SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF 1H-SUBSTITUTED 2, 4, 5- TRIPHENYL IMIDAZOLE DERIVATIVES

Dissertation submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

Chennai - 600 032

In partial fulfillment of the requirements

For the award of the degree of

MASTER OF PHARMACY

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DEPARTMENT OF PHARMACEUTICAL CHEMISTRY

COLLEGE OF PHARMACY

MADURAI MEDICAL COLLEGE

MADURAI – 625 020.

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Madurai -20.

CERTIFICATE

This is to certify that the dissertation entitled – **SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF 1H-SUBSTITUTED 2,4,5- TRIPHENYL IMIDAZOLE DERIVATIVES** was done by **Ms. E. AJILA (Reg.No.261215751)** in the Department of Pharmaceutical Chemistry, College of Pharmacy, Madurai Medical College, Madurai- 625020, in partial fulfillment of the requirement for the Degree of Master of Pharmacy in Pharmaceutical Chemistry under guidance and supervision of **Prof. (Mrs.) R.THARABAI, M.Pharm.,** HOD**,** Department of Pharmaceutical Chemistry in the academic year 2013-2014.

The dissertation is forwarded to the Controller of Examination, The Tamil Nadu Dr.M.G.R. Medical University, Chennai.

Station: Madurai.

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Prof. (Mrs.) R. THARABAI, M.Pharm.

Evaluation certificate

Internal Examiner

External Examiner

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I express my sincere thanks to **Prof. Dr. A. ABDUL HASAN SATHALI, M.Pharm, PhD.,** Principal I/C,& Head of the Department of Pharmaceutics ,College of Pharmacy, Madurai Medical College,Madurai for the support and encouragement for my project work.

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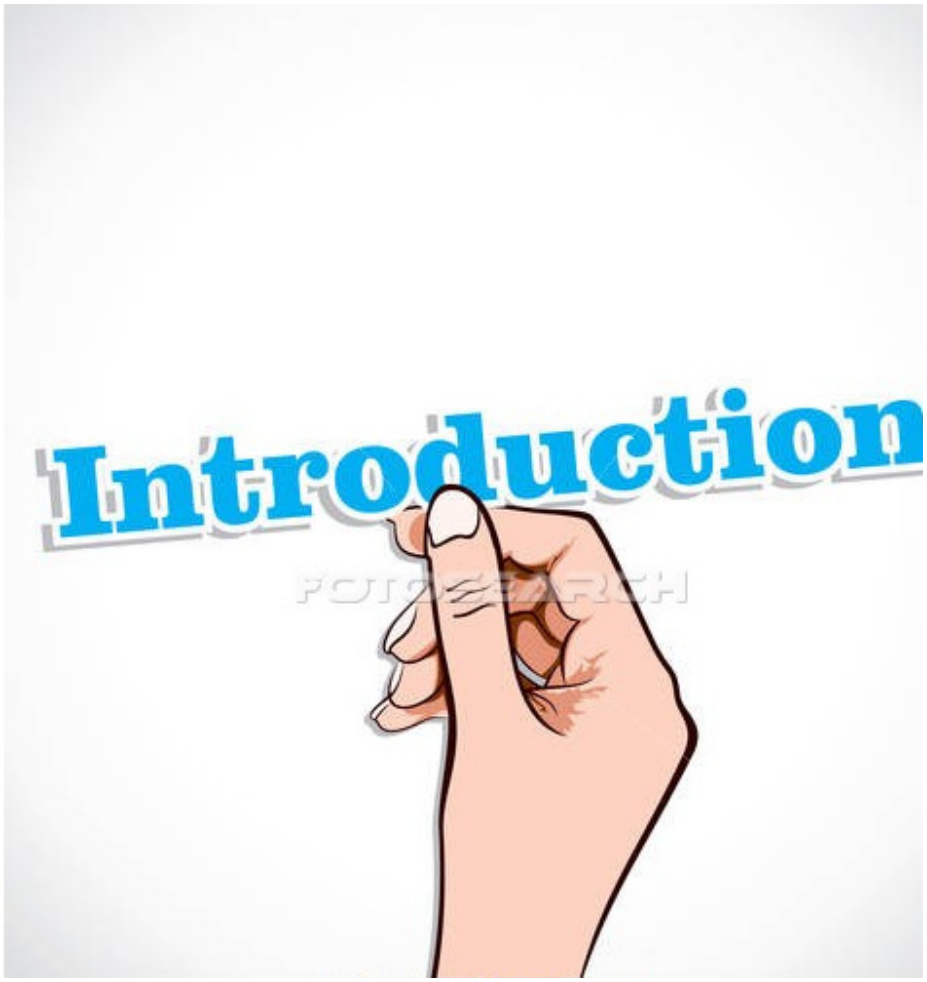
CONTENTS

DETAILS OF ABBREVIATION

°C	:	Degree Centigrade
%	:	Percentage
Gm	:	Gram
mg	:	Milligram
mol	:	Mole
Ar	:	Aromatic
Rf	:	Retention factor
Str	:	Stretching
DMSO	:	Dimethyl sulfoxide
Mm	:	Millimeter
M.wt	:	Molecular weight
M.F	:	Molecular formula
Ph	:	Hydrogen in concentration
NMR	:	Nuclear Magnetic Resonance
mts	:	minutes
ppm	:	Parts per million
BSA	:	Bovine Serum Albumin


Introduction

INTRODUCTION

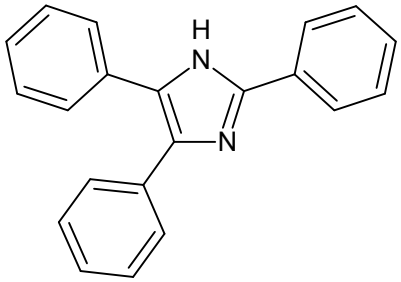
MEDICINALCHEMISTRY

Medicinal chemistry is a chemistry based discipline, also involving aspects of biological, medical and pharmaceutical sciences. It is concerned with the invention discovery, design, identification and preparation of biologically active compounds, the study of their metabolism, the interpretation of their mode of action at the molecular level and construction of structural activity relationship.

Medicinal chemistry involves the lead molecules potency, selectivity, reduce toxicity, pharmacokinetic and pharmaceutical properties. It is a science whose roots lie in all branches of chemistry and biology. The earlier sources of drugs were from plants, animals and mineral but due to the lack of potential action and definitive cure and some time more toxicity, the discovery of new drugs that are more potential and less toxic is essential. The synthesis of derivatives has been an important part and is aimed at modifying the action of drugs, particularly to reduce the side effects and to potentiate the drug action. Today more than 60% drugs used in practice are synthesized derivatives and day by day the scope of synthetic medicinal chemistry is broadening.

Once of new pharmaceutical lead compound has been discovered, extensive and costly efforts usually are made to prepare a series of analogue in the hope that even better activity will be found such programs included the branching, lengthening or shortening of chain structure, the variation of the kinds and positions of substituent's the replacement of rings by similar cyclic structures and other empirical molecular modifications within the frame work of reasonably close analogue.

TRIPHENYL IMIDAZOLE[9,19]



Imidazoles are probably the most well known heterocycle which is common and important feature of a variety of natural products and medicinal agents.

The compound$C_{21}H_{16}N_2$, has been known since 1877. Although the crystal structure of 36 derivatives of lophine are known, the structure of parent compound has remained unknown until now.

The three phenyl rings bonded to the imidazole core are not coplanar with the latter, with dihedral angles of 21.4 (3), 24.7 (3), and 39.0 (3)°, respectively, between the phenyl ring planes in the 2-, 4- and 5-positions of the imidazole ring. The molecules are packed in layers running perpendicular to the *b* axis. There are acceptor and donor atoms for hydrogen bonds.

The synthesis of novel 2,4,5-triphenylimidazole derivatives seems to be main focus of the medicinal research because compounds containing triphenyl imidazole moiety provides a number of needful biological activities such as analgesic and antiinflammatory activities (Shallini *et al.*, 2011; Achar *et al.,* 2010). Antiinflammatory activity (Yasodha *et al*., 2009). The substitution at C-2 benzene nucleus with benzyl, benzoyl, para amino benzoyl antifungal activity (Yadav *et al*., 2011). The 2,4,5-triphenyl nucleus had been synthesized by microwave technique as well (Pandit *et al*., 2011). The trimethoxy benzene nucleus at the 2 position of imidazole ring in antiinflammatory and antifungal activities (Umarani *et al.,* 2011). Addition of thiol group in 2,4,5-triphenylimidazole in increased activity (El Ashry *et al*., 2007).

Azole ring in place of abstractable hydrogen in 2,4,5-triphenylimidazole ring potent antibacterial and antiinflammatory activity (Amir *et al*., 2011).

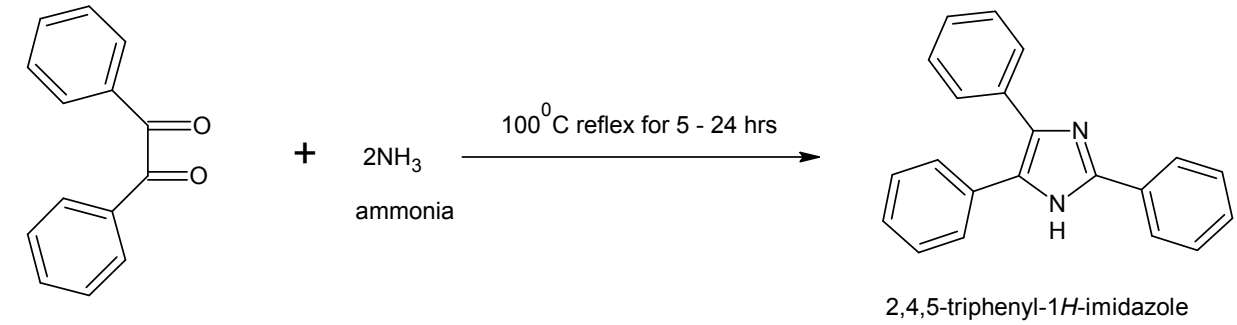
On the basis of various literature surveys Imidazole derivatives shows various pharmacologicalactivities

- Anti fungal and Anti-bacterial activity
- Anti inflammatory activity and analgesic activity
- Anti tubercular activity
- Anti depressant activity
- Anti cancer activity
- Anti viral activity
- Antileishmanial activity
- Anti arthritic activity
- Anti angiogenesis

In this present study 1-H substituted 2,4,5 triphenyl imidazole derivative are designed, synthesized and their biological activities were screened.

METHODS OF TRIPHENYL IMIDAZOLE PREPARATION

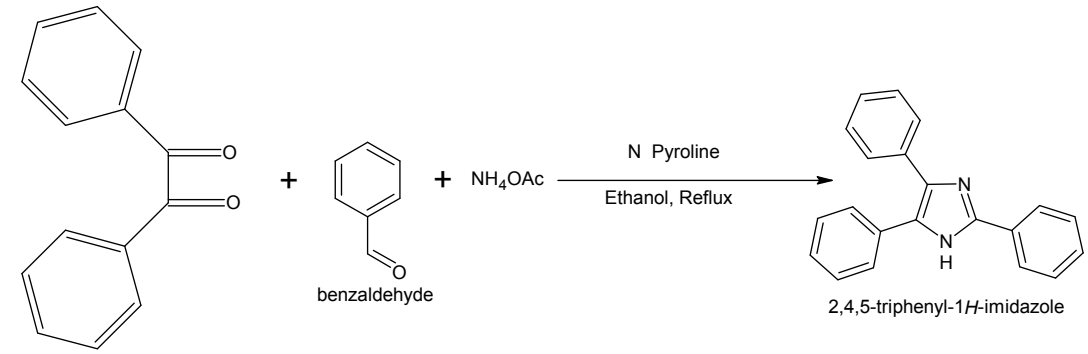
1) CONVENTIONAL HEATING: BURUNGALE SWATI *et al*., (2013)



1,2-diphenylethane-1,2-dione

2,4,5-triphenyl-1*H*-imidazole

2) CATALYST USED : NANA V.SHITOLE *et al*., (2009)

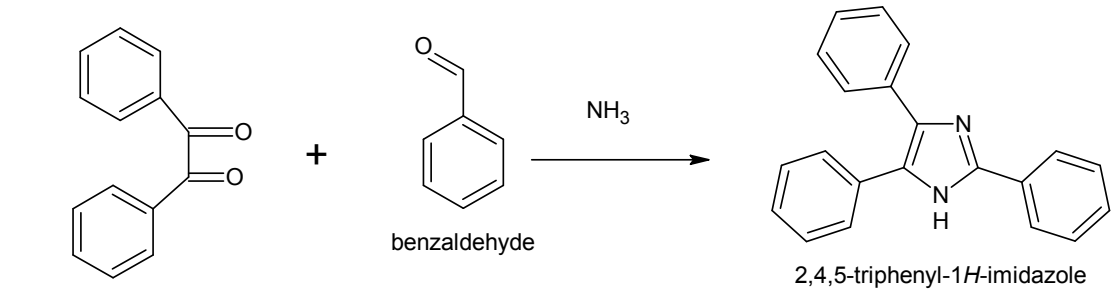


1,2-diphenylethane-1,2-dione

benzaldehyde

2,4,5-triphenyl-1*H*-imidazole

3) RADISZEWSKI SYNTHESIS:



1,2-diphenylethane-1,2-dione

benzaldehyde

2,4,5-triphenyl-1*H*-imidazole

MOLECULAR DESIGN

Molecular design is the process of finding new medicines based on the knowledge of a biological target, it enabled the chemist to predict the structure and the value of certain properties of various compounds.

It also allows the medicinal chemist to evaluate the interaction between a compound and its target site before synthesizing a compound so as to increase the ability by reducing the side effects.

VARIOUS SOFTWARE USED IN MOLECULAR DESIGN:

- CHESKETCH
- CHEMDOODLE
- MOLINSPIRATION
- **LIPINSKI`S RULE:**
    - Molecular weight should be less than 500.
    - Log p value should be less than 5.
    - Number of H-bond donors should be less than 5.
    - Number of H- bond acceptor should be less than 5.
    - Molar refractivity should be less than 150.

SPECTROSCOPY[45,46,48,49]

Study of interaction of electromagnetic radiation with various matters.

METHOD	PRINCIPLE AND APPLICATION	MOLECULAR PHENOMENON
INFRARED SPECTROSCOPY	Structure determination and identity of organic and inorganic compounds, generally quantitative analysis.	Excitation of molecular vibrations by light absorption.
HNMR SPECTROSCOPY	Structure determination and identity organic compounds, molecular conformation.	Re-orientation of magnetic nuclei in a magnetic field.
MASS SPECTROSCOPY	Structure determination and identity of organic compounds, analysis of trace volatiles in non volatiles.	Ionization of molecules and cracking of molecules into fragment ion.

ANTIBACTERIAL ACTIVITY[21,25,42,51-53]

Antibacterial agents:

The drug which inhibits or destroys the growth of bacteria

ORGANISM USED FOR ACTIVITY:

Bacillus subtilis:

- Gram positive bacteria.
- Rod shaped
- Responsible for food- borne illness.

Klebsiella pneumonia:

- Gram negative bactria.
- Non motile
- Infection of surgical wounds &respiratory tract

Mechanism:

Antibacterial agents inhibit

- Cell wall synthesis
- Protein synthesis
- Nucleic acid synthesis
- Enzymatic activity
- Folate metabolism

Evaluation methods:

- Turbidimetric method
- Agar cup plate method

ANTIFUNGAL ACTIVITY[21,25,42,51-53]

Antifungal agents:

The drugs which are inhibit or destroy the growth of fungus.

Candida albicans:

- It causes cutaneous candidiasis
- Infections found in genitals
- Spread by direct or sexual contact
- Prevented by means of hygiene

Aspergillusniger:

- It causes Aspergillosis
- It causes black molds on fruits and vegetables
- Common symptom is fungal ear infection

Mechanism:

- Cell membrane disruption
- Inhibition of cell division
- Inhibition of cell wall formation

Evaluation methods:

- Turbidimetric method
- Agar cup-plate method

ANTI-OXIDANT [54,56,57]

Antioxidants are chemicals that block the activity of other chemicals known as free radicals.

Antioxidants are chemicals that interact with and neutralize free radicals thus preventing them from causing damage. Antioxidant is also known as free radical scavengers.

Antioxidants are compounds in foods that neutralize chemicals (free radical) produced by oxidation in the human body. These have been linked to disease such as heart and liver disease and cancer.

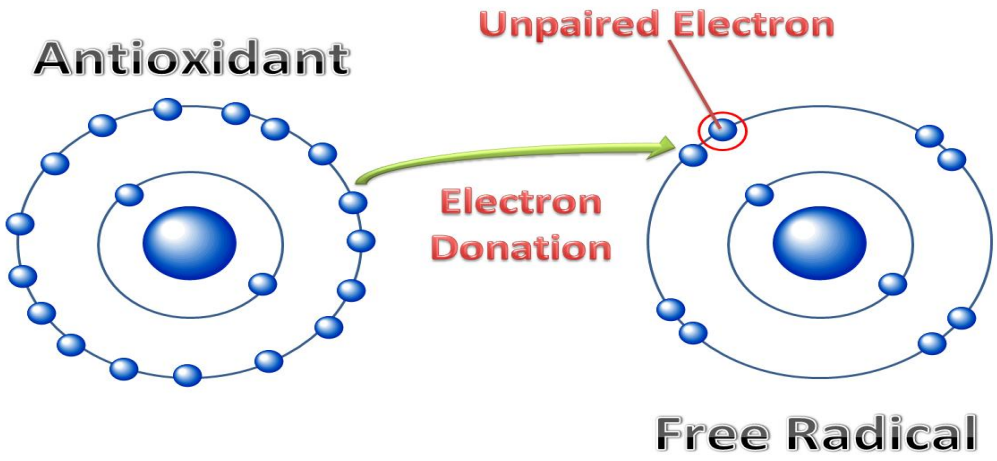
The process of oxidation in the human body damage cell membranes and others structures including cellular proteins lipids and DNA. When oxygen is metabolized it creates unstable molecules called free radicals.

The effect of free radicals:

- Deterioration of the eye lens which contributes to blindness
- Inflammation of the joints
- Damage to nerve cells in the brain
- Acceleration of the ageing process
- Increased risk of coronary heart disease since free radicals encourage low density.
- Lipoprotein(LDL) cholesterol to stick to artery walls
- Certain cancers triggered by damage cell DNA.

Source of antioxidant:

- Fruits
- Vegetables
- Meats
- Poultry
- Fish



ANTI-ARTHRITIS [27,38,40,56]

Definition:

It is a form of joint disorder that involves inflammation of one or more joints.

Type of arthritis:

There are over 100 different form of arthritis.

The most common from

- Autoimmune disease:
  - Rheumatoid arthritis
  - Psoriatic arthritis
- Osteoarthrititis

❖ **Autoimmune disease**:

Rheumatoid arthritis:

Is an autoimmune disease in which there is joint inflammation, synovial proliferation and destruction of articular cartilage. Immune complexes composed of Igm activate complement and release cytokines which are chemotactic for neutrophils. These inflammatory cells secrete lysosomal enzymes which damagecartilage and erode bone, while PGS produced in the process cause vasodialation and pain.

Psoriasis :

Develop into psoriatic arthritis. With psoriatic arthritis, most individuals develop the skin problem first and then the arthritis. The typical features are of continuous joint pains,

stiffness and swelling. The disease does recur with periods of remission but there is no cure for than disorder.

Osteoarthritis:

Is an degenerative joint disease. In the aged and children, pain might not be the main presenting feature; the aged patient simply moves less, the infantile patient refuses to use the affected limb.

- **Causes:**
  - Joint pain
  - Inflammation
  - Muscle strain
  - Weight loss
  - Poor sleep
  - Tenderness
- **Symptoms:**
  - Joint pain tenderness and stiffness
  - Inflammation and around the joints
  - Restricted movement of the joint
  - Warmth and redness of the skin
  - Weakness and muscle wasting

ANTI – ANGIOGENESIS[55-58]

Definition:

Angiogenesis is the process of making new blood vessels.

The term comes from two Greek words, angio meaning blood vessel, and genesis meaning beginning.

Angiogenesis is first named by Herting in 1935, mechanism revealed by Folkman.

When potential anti- angiogenesis drug were first tested in the lab in the late 1990s

Anti- angiogenesis is a form of targeted therapy that uses drugs or other substances to stop tumors from making new blood vessels. Without a blood supply tumors can't grow.

One promising cancer treatment to come from this research is called anti-angiogenesis.

Hope of Angiogenesis:

- Drugs might replace chemotherapy
- Offering a more effective
- Less toxic way to treat cancer

Types of anti angiogenesis treatment:

1) Drugs that block blood vessel growth factor

Some drugs block vascular endothelial growth factor (VEGF) from attaching to the receptors on the cells that line blood vessels. This stops the blood vessels from growing.

2) Drugs that block signaling within the cell

Some drugs stop the VEGF receptors from sending growth signals into the blood vessel cells. These treatments are also called cancer growth blockers or tyrosine kinase inhibitors.

3) Drugs that effect signals between cells

Some drugs act on the chemicals that cells use to signal to each other to grow. This can block the formation of blood vessels.

Different type of cancer treatment:

1) Chemotherapy
2) Gene therapy
3) Immune therapy
4) Oncogenes and tumor suppressor gene
5) Oral chemo therapy

Uses:

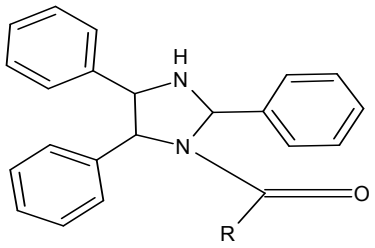
- Wound healing
- Reproductive function
- Diabetes retinopathy
- Arthritis

LITERATUE REVIEW

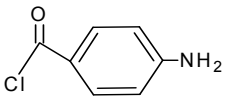
LITERATURE REVIEW

1) Burungale and bhitre *et al.*, (2013),

Synthesis of 2,4,5triphenyl imidazole derivatives and biological evaluation for their antibacterial and anti inflammatory activity.

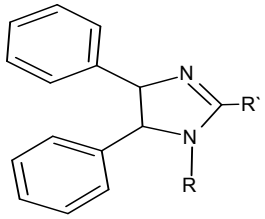


R=



2) Sharma *et al.*, (2013),

Microwave irradiated synthesis of some substituted imidazole derivatives as potential antibacterial and anticancer agents.



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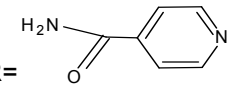

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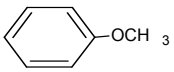
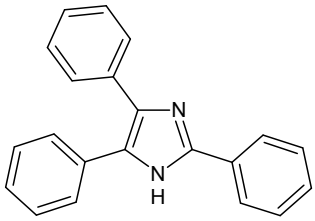


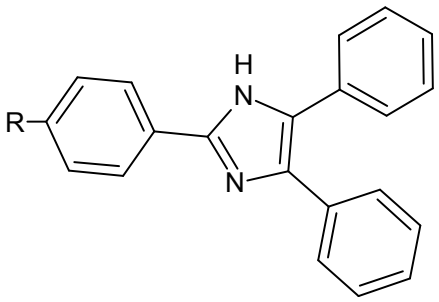
3) Burungaleswati *et al.*, (2013),

Synthesis of 2,4,5triphenyl imidazole derivatives and biological evaluation for their analgesic and anti-inflammatory activity.



4)Kumar Vikrant *et al.*, (2012),

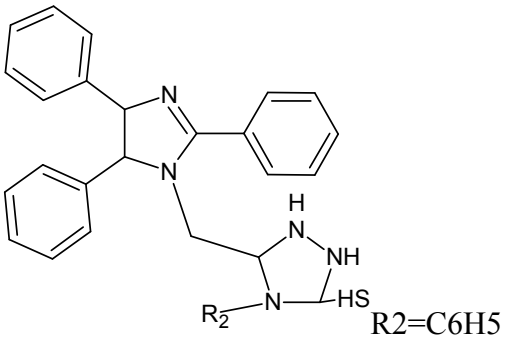
A robust and reliable one pot synthetic method has been developed for 2,4,5 tri substituted imidazole the synthetic sequence via, a multi – component condensation catalyzed by p- toluene sulfonic acid, provides good isolated yields under mild conditions.



R=H,CH3,OCH3,Cl

5) Rajeev Kharb *et al*., (2012),

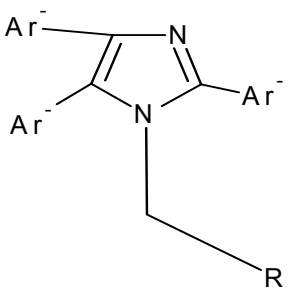
Synthesis and spectral characterization and anthelmintic evaluation of some novel imidazole bearing triazole derivatives.



R2=C6H5

6) S.M. Ahmed *et al*., (2012),

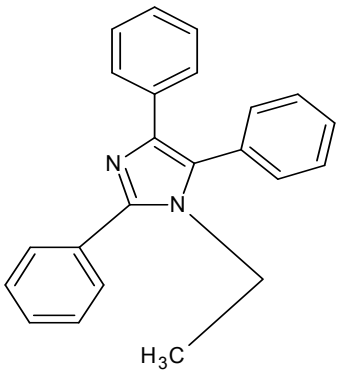
Synthesis and screening of 1H- substituted 2,4,5triphenyl imidazole derivatives.



R=N,NDiethylamine

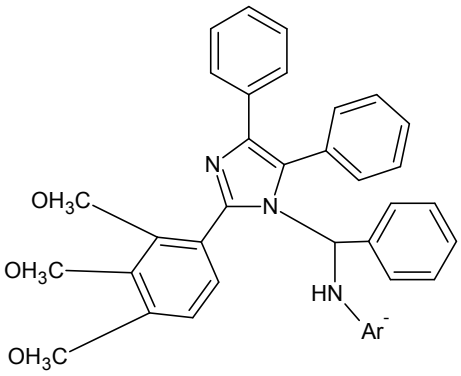
7) RashmiArora *et al* .,(2012),

Synthesis of 2,4,5triphenyl imidazole novel mannich bases as potential anti-inflammatory and analgesic agents.



8) AK.Rathod *et al*., (2012),

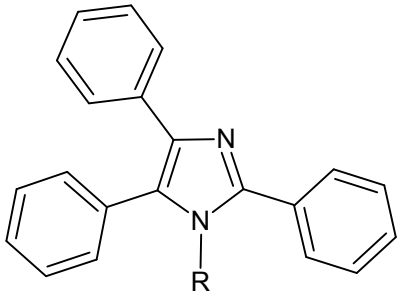
Microwave assisted synthesis and characterization of triphenylimidazolyl derivatives and their antifungal and anti inflammatory activity.



Ar= Diphenylamine

9) Adel A. Marzoak *et al*., (2012),

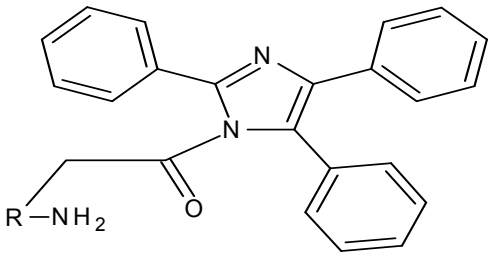
Synthesis of 2,4,5triphenyl imidazole derivatives using diethyl ammonium hydrogen phosphate as green, fast reusable catalyst.



R=Acidic ionic liquids

10) ShaileshP.Zala *et al*., (2012),

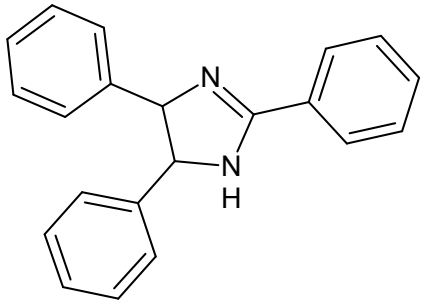
Synthesis and biological evaluation of 2,4,5triphenyl 1H- imidazole-1-yl derivatives.Biological activity of anti inflammatory andante microbial activity.



R=Methoxy benzene

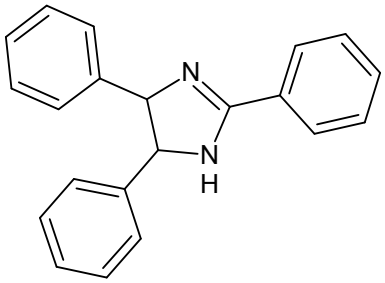
11) Shahedali *et al*., (2011),

Synthesis and characterization of novel series of the imidazoles under solvent free conditions by using sodium dihydrogen phosphate.



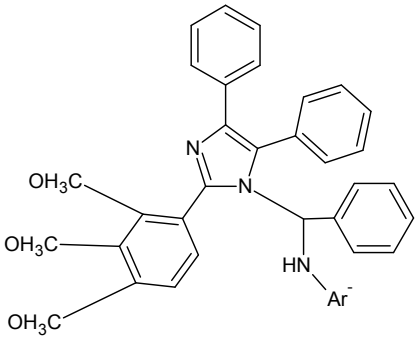
12) Yadav *et al*., (2011),

Synthesis, spectral characterization and biological screening of some novel synthesized imidazoles.

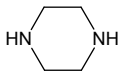


13) N.Umarani *et al.*, (2011),

Exploring the effects of newer three component aminobenzylated reaction of triphenyl imidazole motif as potent antimicrobial and anti-inflammatory agents.

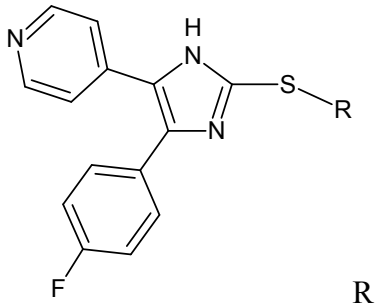


Ar =



14) BhartiAshish*et al.*, (2011),

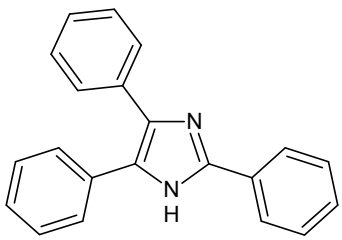
Various approaches for synthesis of imidazole derivatives.Inhibition of cytokine release.



R =CH3

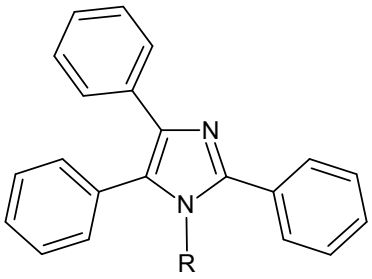
15) Bhatnayar *et al.*, (2011),

A review of on imidazole their chemistry and pharmacological potentials.



16) Javad safari *et al.*, (2010),

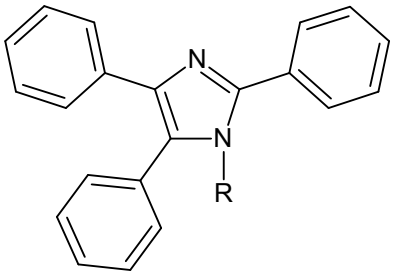
A novel and an efficient catalyst for one pot synthesis of 2,4,5 tri substituted imidazoles by using microwave irradiation under solvent free conditions.



R =C6H5

17) E.Rajanarendar *et al.*, (2010),

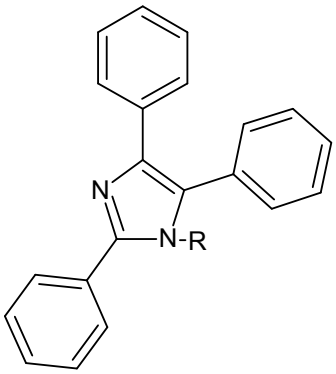
A mild and efficient four component one pot synthesis of 2,4,5triphenyl –(1H-imidazolyl) isoxazole catalyzed by cerric ammonium nitrate.



R =H,Cl

18) Yasodha *et al.*, (2009),

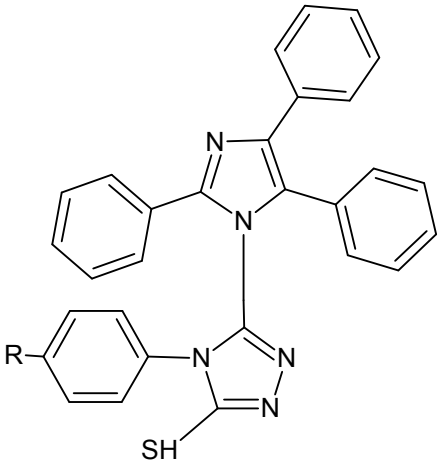
Synthesis and biological evaluation of some 2,4,5triphenyl imidazole derivative and chloro compound of anti-inflammatory and anti microbial activity.



R =Cl

19) Mohd Amir *et al.*, (2009),

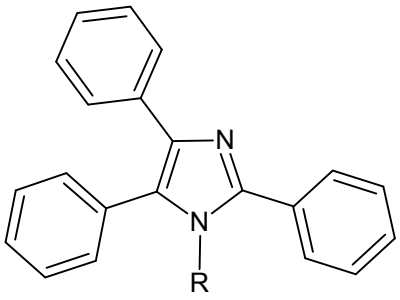
Design and synthesis of some azole derivatives containing 2,4,5triphenyl imidazole moiety as anti inflammatory and antimicrobial agents.



R= CH3

20) Nana V.Shitole *et al.*,(2009),

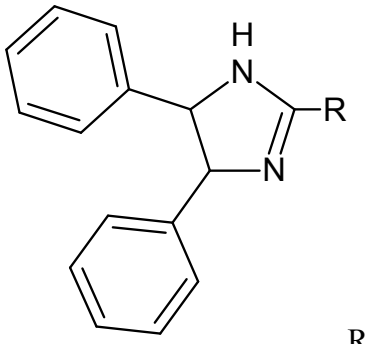
L proline as an efficient catalyst for the synthesis of 2,4,5triaryl -1H- imidazoles.



R=CH3

21) Deana Wahyuningrum *et al*., (2008),

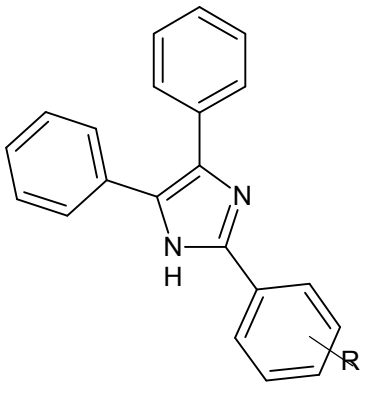
The correlation between structure and corrosion inhibition activity of 4,5 Diphenyl -1-vinyl imidazole derivative compounds towards mild steel in 1% sodium chloride solution.



R = C6H5

22)Arshiaparveen *et al.*,(2007)

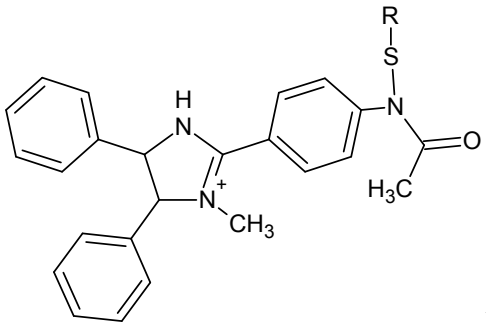
Efficient synthesis of 2,4,5triaryl substituted imidazoles under solvent free conditions at room temperature.



R=H

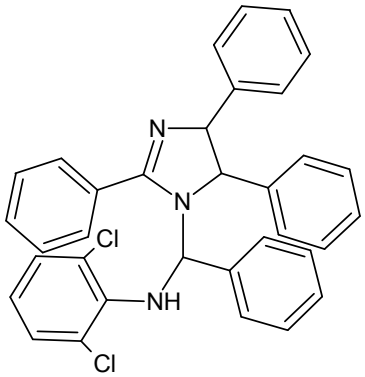
23) Yusuf ozkay *et al.*,

Synthesis and biological evaluation of 2,4,5triphenyl imidazole derivative.

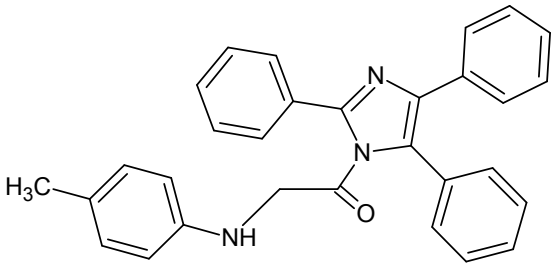


R =CH3

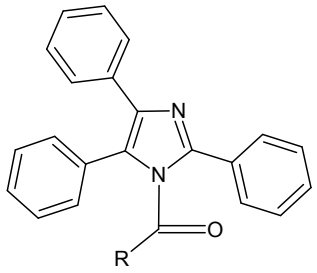
24) A series of N-((2-substituted phenyl)-4,5-diphenyl-1H-imidazol-1yl)(phenyl)methyl) substituted amine derivatives have been synthesized by 2-substituted 4,5-diphenyl imidazole derivatives starting from benzyl and aromatic aldehyde. The newly synthesized compounds were screened for analgesic and anti-inflammatory activities.



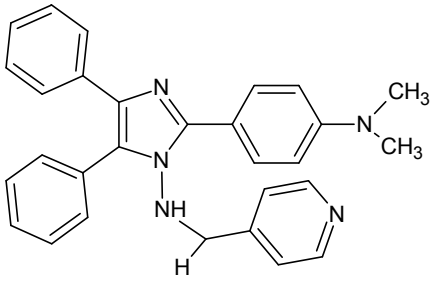
25) A series of 2, 4,5 triphenyl-1H-imidazole-1-yl derivatives have been synthesized and tested for their antiinflammatory activity *in vitro* using Phenylbutazone as a reference drug and antimicrobial activity using clotrimazole and ciprofloxacin as a standard drug. All the synthesized compounds were screened for their anti-fungal activity against *Candida albicans*and for antimicrobial activity against *B. subtilis*and *E. coli*. Compound 8 was found to be the most potent derivative of the series.



26) Radiszewski reported the condensation of a dicarbonyl compound, benzil, and keto aldehyde, benzaldehyde, or diketones in the presence of ammonia yield 2,4,5triphenyl imidazole.

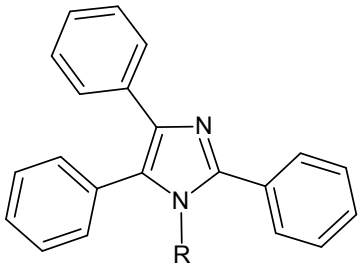


27) A new aryl imidazoles incorporated with chemotherapeutic pharmacophores have been synthesized and evaluated for their anti bacterial and short term anti cancer activity. All the synthesized substituted imidazoles have shown good antibacterial activity against gram negative bacterial strains *Klebsiellapneumoniae* and *Escherichia* Coli.



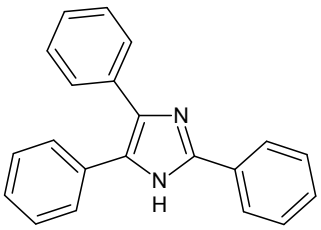
28)**Safari *et al.*,**

Ammonium Molibidate was used as an efficient catalyst for an improved and rapid synthesis of 2,4,5 trisubstituted imidazoles by a three component, one pot condensation of benzyl, aryl aldehyde, ammonium acetate in good yield under solvent free condition using microwave irradidation.



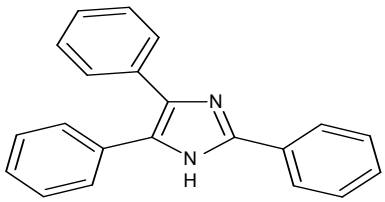
29) **Satyajit *et al.*,**

A series of 2- substituted 4,5diphenyl imidazole were synthesized by refluxing bezil with differrent substituted aldehydes in the presence of ammonium acetate and glacial acetic acid. Compounds were screened for anthelmintic activity.

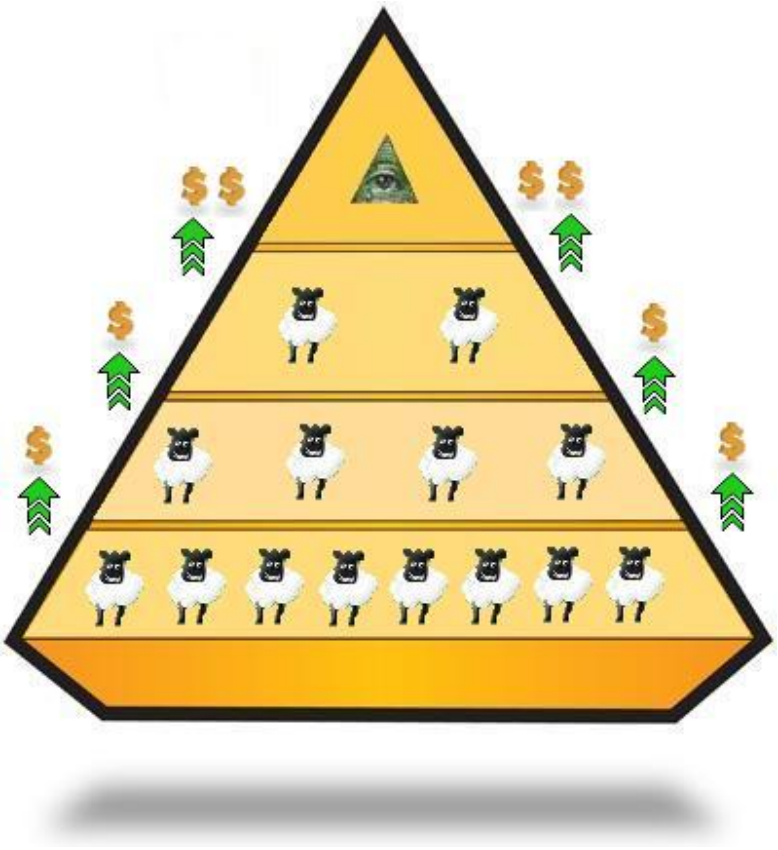


30) **Marzoukadel *et al.*,**

Synthesisof 2,4,5triphenyl imidazole derivative using diethyl ammonium hydrogen phosphate as green fast and reusable catalyst.



AIM AND OBJECTIVE



AIM AND OBJECTIVE

AIM OF PRESENT STUDY:

Triphenylimdazole is a best nucleus and biologically active molecule. Now a day this is interesting research nucleus of substituted derivative.

The aim of the present study was to obtain triphenyl imidazole as biologically effective agent with good therapeutic values and minimum toxic levels.

Past few years most of the research fellowship has done the project in triphenylimidazole by the substitution of primary amine in the position of 1H group in imidazole. But I like to alter the simple modification in the synthesis for evaluate the anti - arthritic anti – oxidant, anti angiogenesis and anti microbial activities.

Step 1

Here I decided to substitute the different aldehyde in the reaction of benzil and ammonium acetate.

Step 2

Here I decided to substitute the different amine in the reaction of triphenyl imidazole and formaldehyde.

OBJECTIVE OF PRESENT WORK:

- **Synthesis:**

  Step I:

  - Synthesis of tri phenyl imidazole derivative.

  Step II:

  - Synthesis of 2,4,5triphenyl -1H-imidazole derivatives (compound A1- A5).
  - Synthesis of 5-(chlorophenyl)-2,4diphenyl -1H-imidazole derivatives (compound A6 –A1).

- **Software used:**

  - Chemskech
  - Chemdoodle
  - Molinspiration

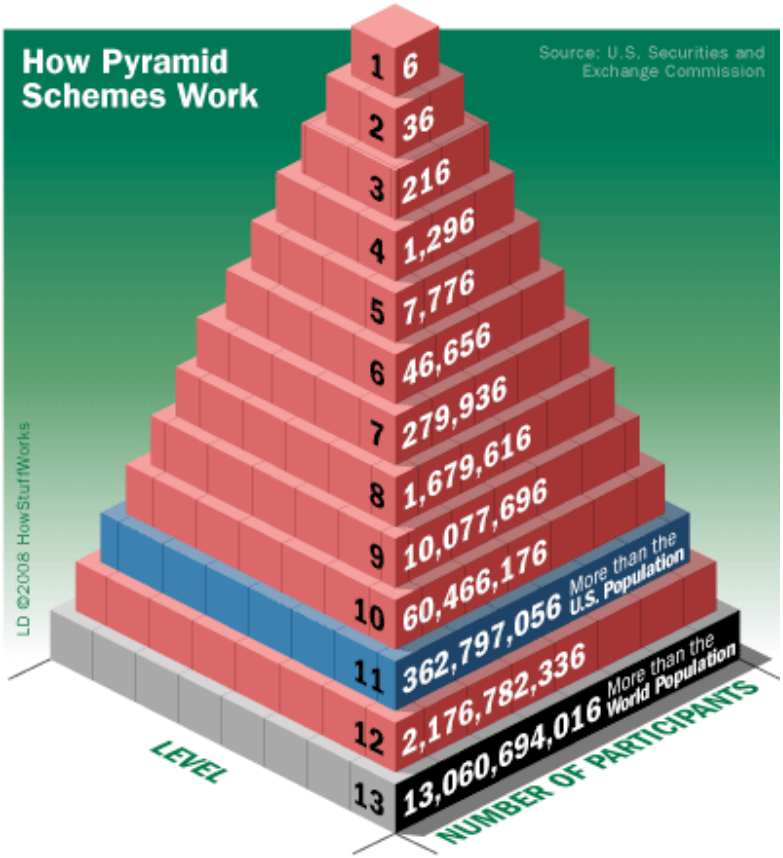
- **Spectral studies**:

  - Infrared spectroscopy
  - Nuclear Magnetic Resonance spectroscopy
  - Mass spectroscopy

- **Biological evaluation:**

  - In vitro Antimicrobial Activity
  - In vitro Antioxidant Activity
  - In vitro Antiarthritic Activity
  - In vivo Antiangiogenesis Activity.

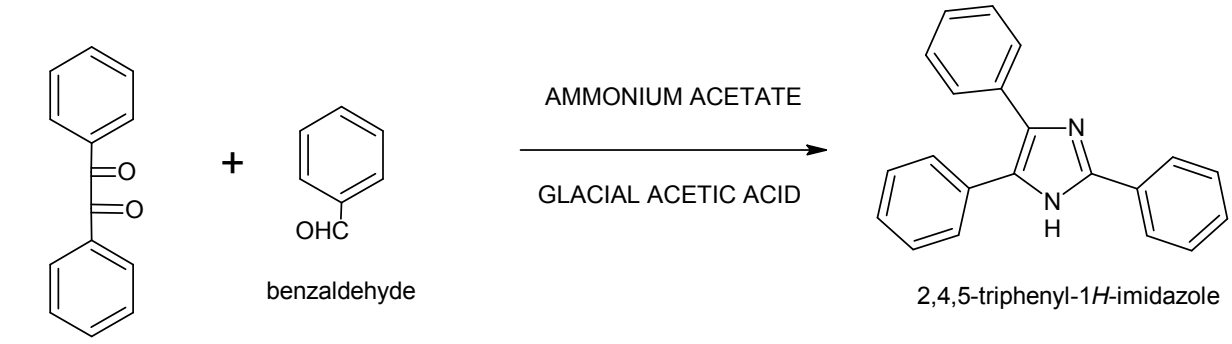
SCHEME OF REACTION



SCHEME OF REACTION

STEP –I PREPARATION OF2,4,5 TRIPHENYL -1H-IMIDAZOLE

COMPOUND A



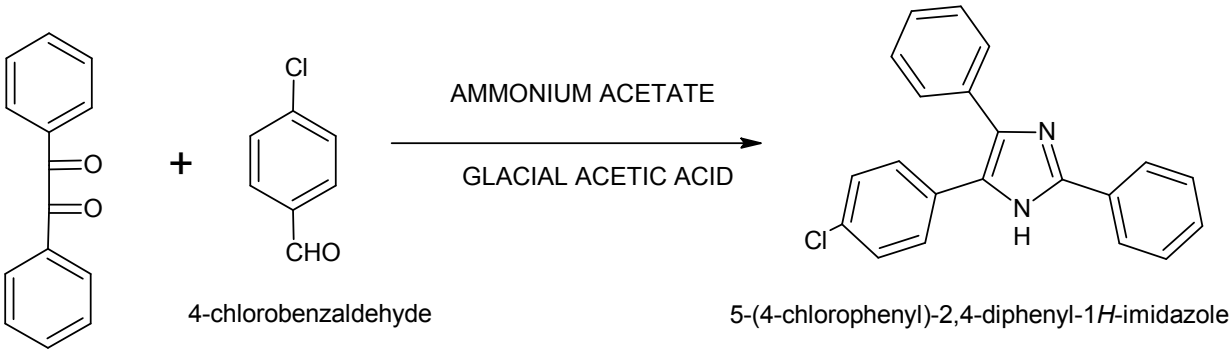
1,2-diphenylethane-1,2-dione

benzaldehyde

2,4,5-triphenyl-1*H*-imidazole

STEP –I PRREPARATION OF 5-(4CHLOROPHENYL)2,4DIPHENYL- 1H-IMIDAZOLE

COMPOUND B



BENZIL

4-chlorobenzaldehyde

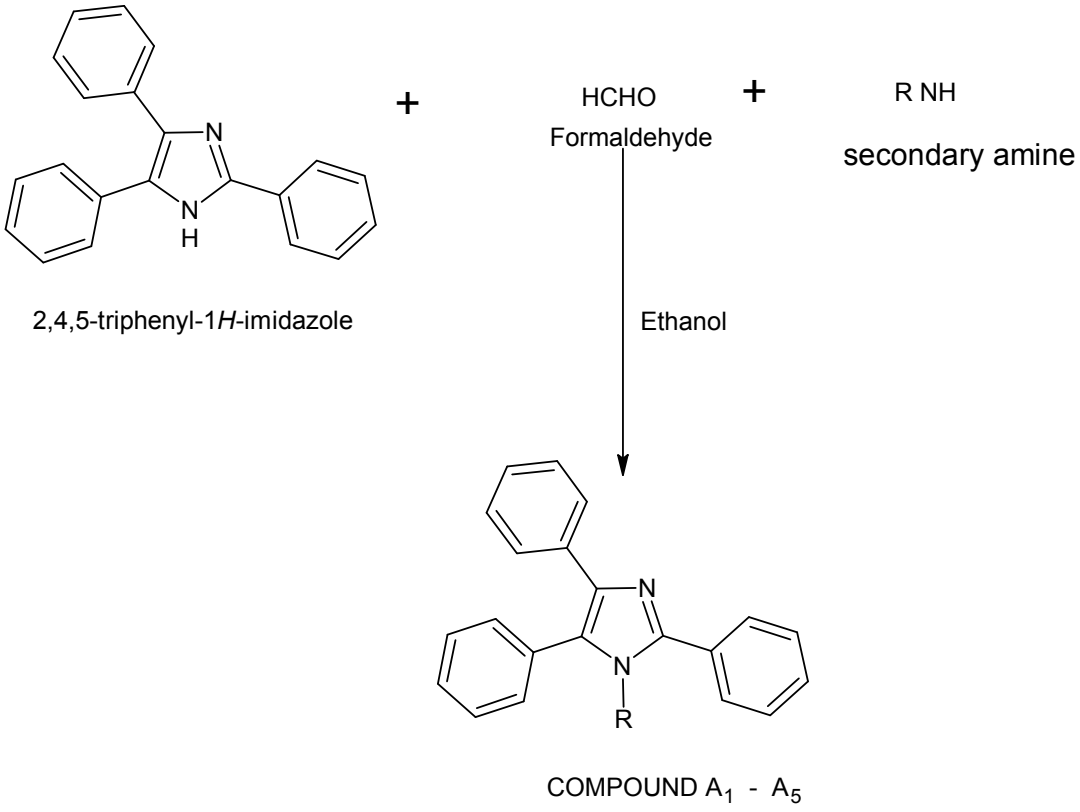
5-(4-chlorophenyl)-2,4-diphenyl-1*H*-imidazole

STEP –II

PREPARATION OF 1H- SUBSTITUTED TRIPHENYL

IMIDAZOLE DERIVATIVES

COMPOUND A1 - A5(A - DERIVATIVE)



COMPOUND A_1 - A_5

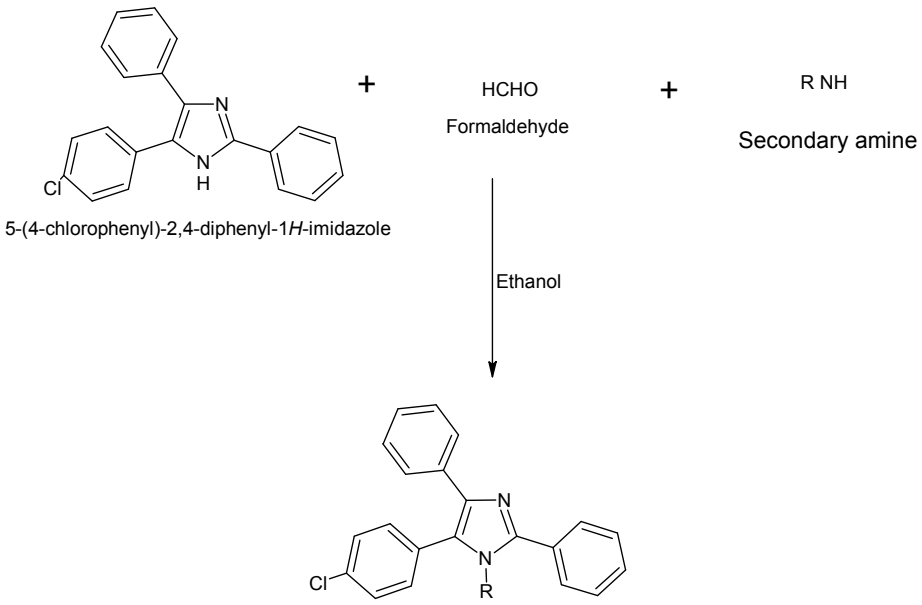
COMPOUND	R
A1	Pyrrole
A2	Piperzine
A3	Diphenyl amine
A4	Pyrrolidine
A5	Dimethyl amine

STEP – II

PREPARATION OF SUBSTITUTED 5-(4-CHLOROPHENYL)-2,4-DIPHENYL-

1H- IMIDAZOLE DERIVATIVES

COMPOUND A6 – A10 (B - DERIVATIVE)



COMPOUND A6 - A10

COMPOUND	R
A6	Pyrrole
A7	Piperzine
A8	Diphenyl amine
A9	Pyrrolidine
A10	Dimethyl amine

EXPERIMENTAL WORK

EXPERIMENTAL PROCEDURE[5,33]

COMPOUND - A

STEP - I

PREPARATION OF 2,4,5 TRIPHENYL -1H- IMIDAZOLE

CHEMICAL REQURIEDS:

Benzil	- 1gm
Ammonium acetate	- 1gm
Benzaldehyde	- 2ml
Glacial acetic acid	- 2ml

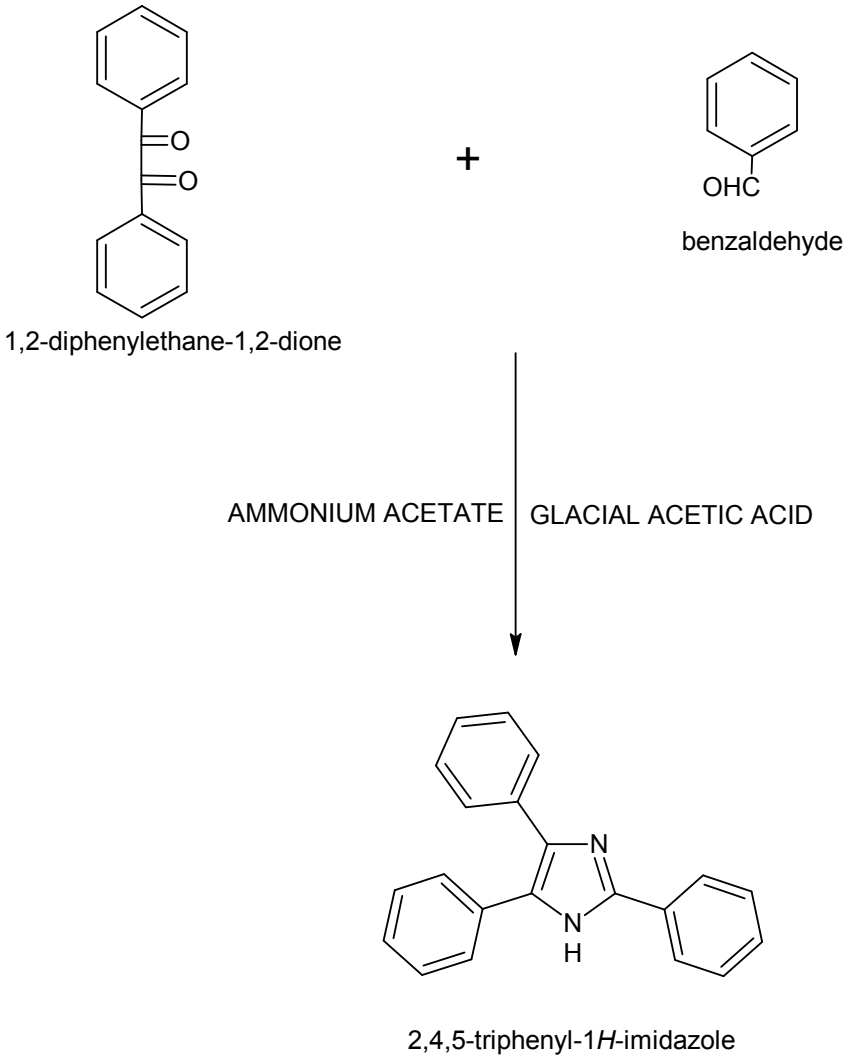
PROCEDURE:

Benzil (1gm),Ammonium acetate (1gm), Benzaldehyde(2ml),Glacial acetic acid(2ml) are reflux for 3hours.the reaction mixture was allowed to stand to attain room temperature. To that add 150 ml of water, the solid thus obtained was filtered. The filterate is neutralized with ammonium hydroxide or sodium carbonate to give solid pasty mass and filtered. Then the solid mass was washed with toluene and recrystalized from methanol.

STEP - 1

COMPOUND - A

PREPARATION OF 2,4,5 TRIPHENYL -1H- IMIDAZOLE



1,2-diphenylethane-1,2-dione

benzaldehyde

2,4,5-triphenyl-1*H*-imidazole

STEP - I

COMPOUND -B

PREPARATION OF 5-(4-CHLOROPHENYL)-2,4-DIPHENYL- 1H- IMIDAZOLE

CHEMICAL REQUIREDS:

Benzil	- 1gm
Ammonium acetate	- 1gm
P-ChloroBenzaldehyde	- 2ml
Glacial acetic acid	- 2ml

PROCEDURE:

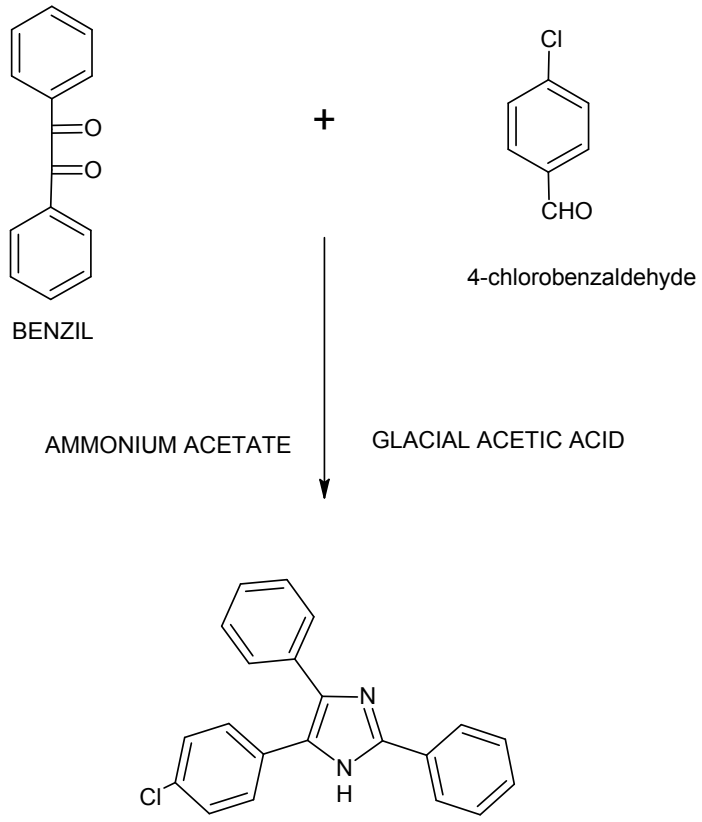
Benzyl (1gm),Ammonium acetate (1gm)P-ChloroBenzaldehyde(2ml),Glacial acetic acid(2ml) are reflux for 3hours.the reaction mixture was allowed to stand to attain room temperature. To that add 150 ml of water, the solid thus obtained was filtered. The filterate is neutralized with ammonium hydroxide or sodium carbonate to give solid pasty mass and filtered. Then the solid mass was washed with toluene and recrystalized from methanol.

STEP - I

COMPOUND -B

***PREPARATION OF* 5-(4-CHLOROPHENYL)-2,4-**

DIPHENYL- 1H- IMIDAZOLE



5-(4-chlorophenyl)-2,4-diphenyl-1*H*-imidazole

STEP -II(COMPOUND A DERIVATIVE)

COMPOUND A1

Synthesis of 2,4,5triphenyl -1-(1H-pyrrol-1-yl) -1H- imidazole

CHEMICAL REQUIREDS:

Triphenyl imidazole - 0.01M

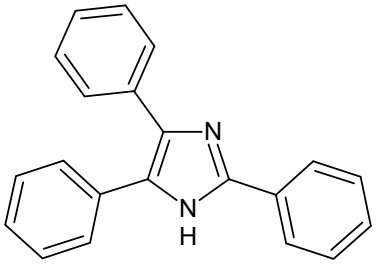
Formaldehyde - 3gm

Ethanol in pyrrole - 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of pyrrole the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

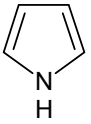
COMPOUND A1



2,4,5-triphenyl-1*H*-imidazole

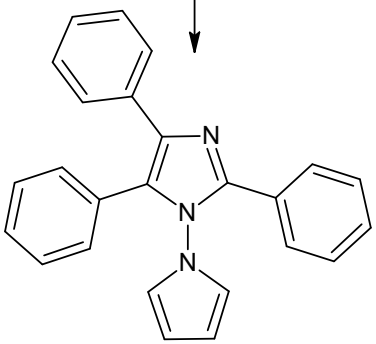
\+ HCHO +

Formaldehyde



1*H*-pyrrole

Ethanol



2,4,5-triphenyl-1-(1*H*-pyrrol-1-yl)-1*H*-imidazole

Molecular Formula	= $C_{25}H_{19}N_3$
Formula Weight	= 361.43846
Composition	= C(83.08%) H(5.30%) N(11.63%)
Molar Refractivity	= 115.98 ± 0.5 cm^3
Molar Volume	= 318.5 ± 7.0 cm^3
Parachor	= 833.6 ± 8.0 cm^3
Index of Refraction	= 1.648 ± 0.05
Surface Tension	= 46.8 ± 7.0 dyne/cm
Density	= 1.13 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 45.98 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 361.157898 Da
Nominal Mass	= 361 Da
Average Mass	= 361.4385 Da

COMPOUND A2

Synthesis of 2,4,5triphenyl -1-(1H-piperzine-1-yl) -1H- imidazole

CHEMICAL REQUIREDS:

Triphenyl imidazole - 0.01M

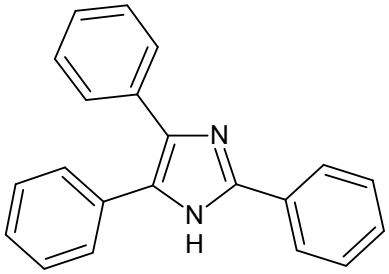
Formaldehyde - 3gm

Ethanol in Piperzine - 10%

PROCEDURE:

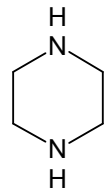
The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of piperzine the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND A2



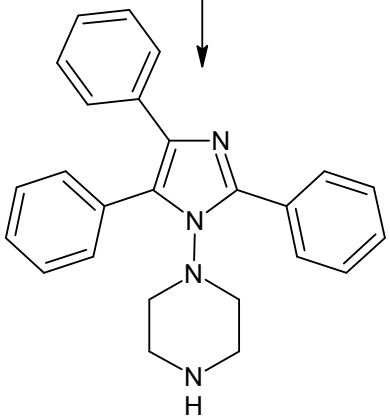
2,4,5-triphenyl-1*H*-imidazole

\+ HCHO Formaldehyde +



piperazine

Ethanol



2,4,5 triphenyl - 1 - (1H piperzine - 1 - yl) - 1H - imidazole

Molecular Formula	= $C_{25}H_{24}N_4$
Formula Weight	= 380.48486
Composition	= C(78.92%) H(6.36%) N(14.73%)
Molar Refractivity	= 119.03 ± 0.5 cm^3
Molar Volume	= 323.2 ± 7.0 cm^3
Parachor	= 853.3 ± 8.0 cm^3
Index of Refraction	= 1.657 ± 0.05
Surface Tension	= 48.5 ± 7.0 dyne/cm
Density	= 1.17 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 47.19 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 380.200097 Da
Nominal Mass	= 380 Da
Average Mass	= 380.4849 Da

COMPOUND A3

Synthesis of N,N diphenyl-2,4,5 triphenyl -1H- Imidazole- 1- amine

CHEMICALS REQUIRED:

Triphenyl imidazole - 0.01M

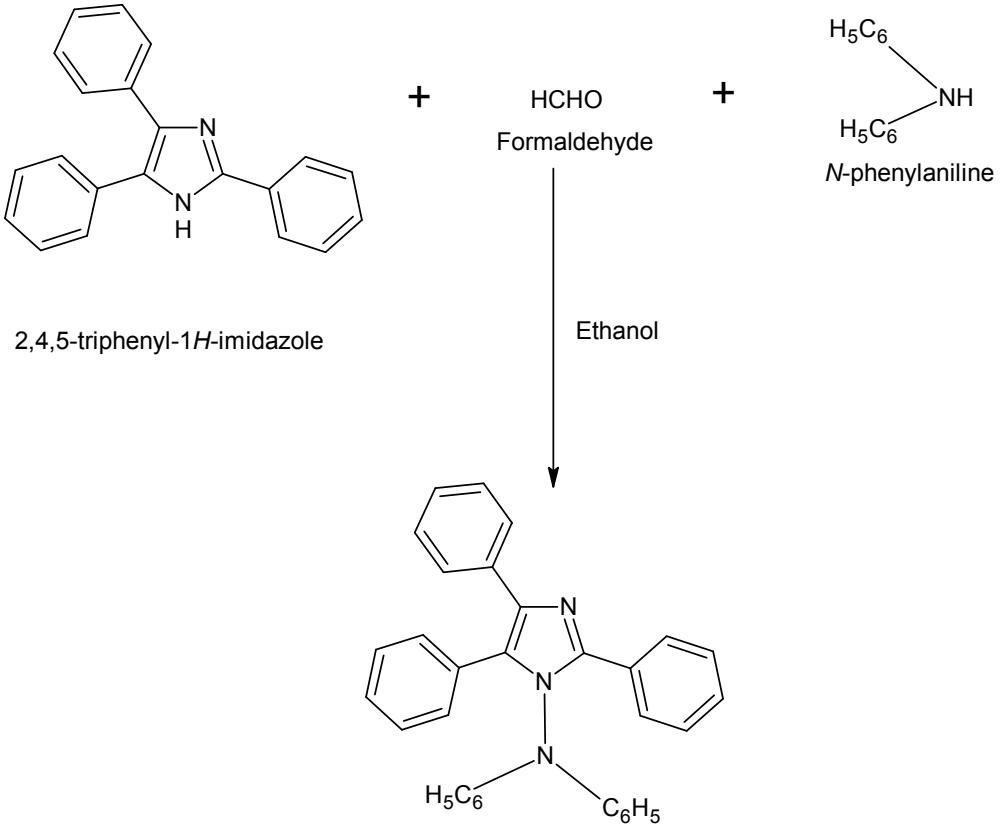
Formaldehyde - 3gm

Ethanol in Diphenyl amine - 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of diphenyl amine the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND A3



2,4,5-triphenyl-1*H*-imidazole

N,N diphenyl - 2,4,5 triphenyl - 1H - imidazol - 1 - amine

Molecular Formula	= $C_{33}H_{25}N_3$
Formula Weight	= 463.5717
Composition	= C(85.50%) H(5.44%) N(9.06%)
Molar Refractivity	= 150.30 ± 0.5 cm^3
Molar Volume	= 418.4 ± 7.0 cm^3
Parachor	= 1087.7 ± 8.0 cm^3
Index of Refraction	= 1.637 ± 0.05
Surface Tension	= 45.6 ± 7.0 dyne/cm
Density	= 1.10 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 59.58 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 463.204848 Da
Nominal Mass	= 463 Da
Average Mass	= 463.5717 Da

COMPOUND A4

Synthesis of 2,4,5triphenyl -1-(1H-pyrrolidin-1-yl) -1H-Imidazole

CHEMICALS REQUIRRED:

Triphenyl imidazole - 0.01M

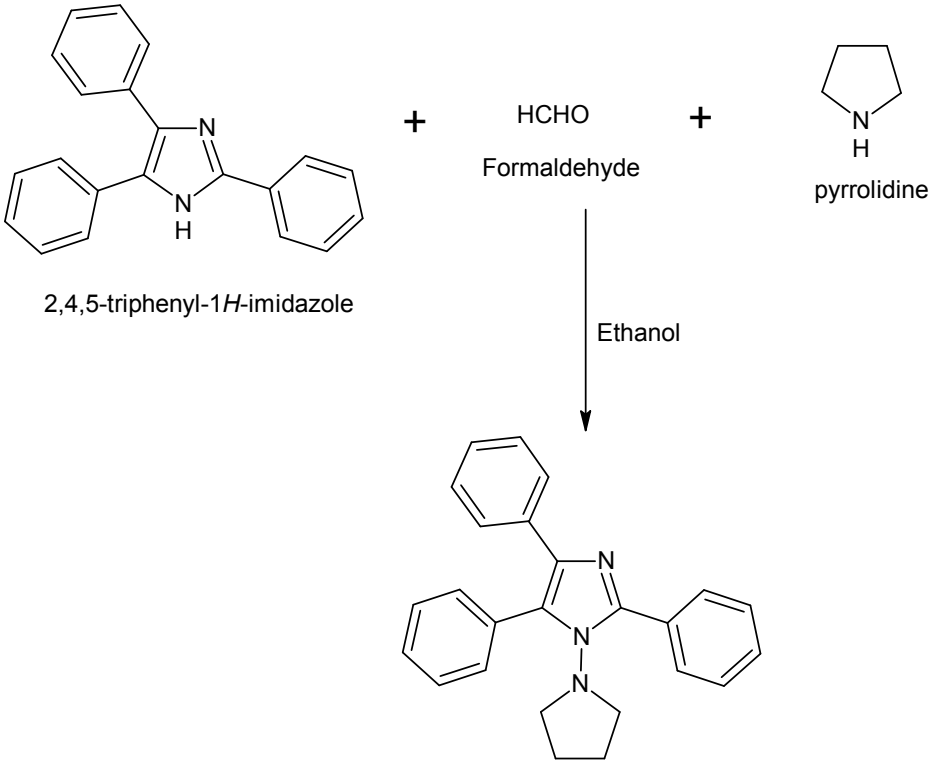
Formaldehyde - 3gm

Ethanol in pyrrolidine - 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of pyrrolidine the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND 4



2,4,5-triphenyl-1*H*-imidazole

2,4,5,triphenyl -1 - (pyrrolidin -1 -yl)-1H - imidazole

Molecular Formula	= $C_{25}H_{23}N_3$
Formula Weight	= 365.47022
Composition	= C(82.16%) H(6.34%) N(11.50%)
Molar Refractivity	= 115.98 ± 0.5 cm^3
Molar Volume	= 318.5 ± 7.0 cm^3
Parachor	= 833.6 ± 8.0 cm^3
Index of Refraction	= 1.648 ± 0.05
Surface Tension	= 46.8 ± 7.0 dyne/cm
Density	= 1.14 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 45.98 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 365.189198 Da
Nominal Mass	= 365 Da
Average Mass	= 365.4702 Da

COMPOUND A5

Synthesis of N,N dimethyl 2,4,5 triphenyl-1H- Imidazol - amine

Triphenyl imidazole - 0.01M

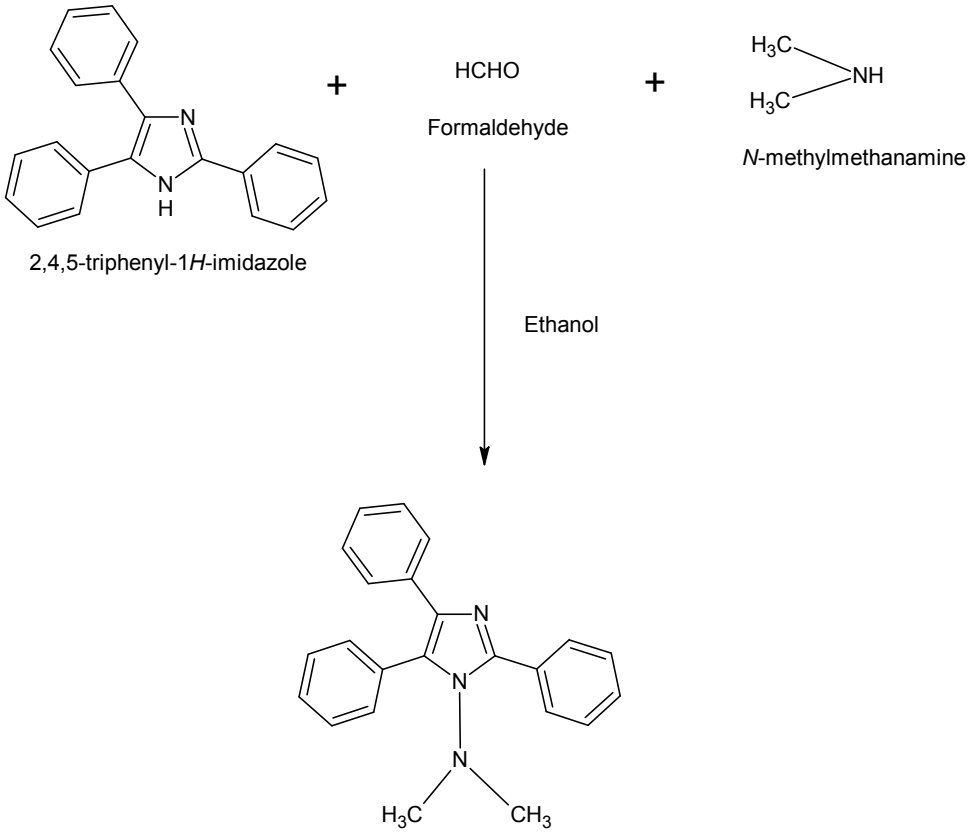
Formaldehyde - 3gm

Ethanol in dimethyl amine - 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of dimethyl amine the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND A5



2,4,5-triphenyl-1*H*-imidazole

N-methylmethanamine

N,*N*-dimethyl-2,4,5-triphenyl-1*H*-imidazol-1-amine

Molecular Formula	= $C_{23}H_{21}N_3$
Formula Weight	= 339.43294
Composition	= C(81.38%) H(6.24%) N(12.38%)
Molar Refractivity	= 108.94 ± 0.5 cm^3
Molar Volume	= 313.2 ± 7.0 cm^3
Parachor	= 796.1 ± 8.0 cm^3
Index of Refraction	= 1.612 ± 0.05
Surface Tension	= 41.7 ± 7.0 dyne/cm
Density	= 1.08 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 43.18 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 339.173548 Da
Nominal Mass	= 339 Da
Average Mass	= 339.4329 Da

STEP - II (COMPOUND B DERIVATIVE)

COMPOUND A6

Synthesis of 5-[4- chlorophenyl2,4, diphenyl -1-(1H-pyrrol-1-yl) -1H- imidazole

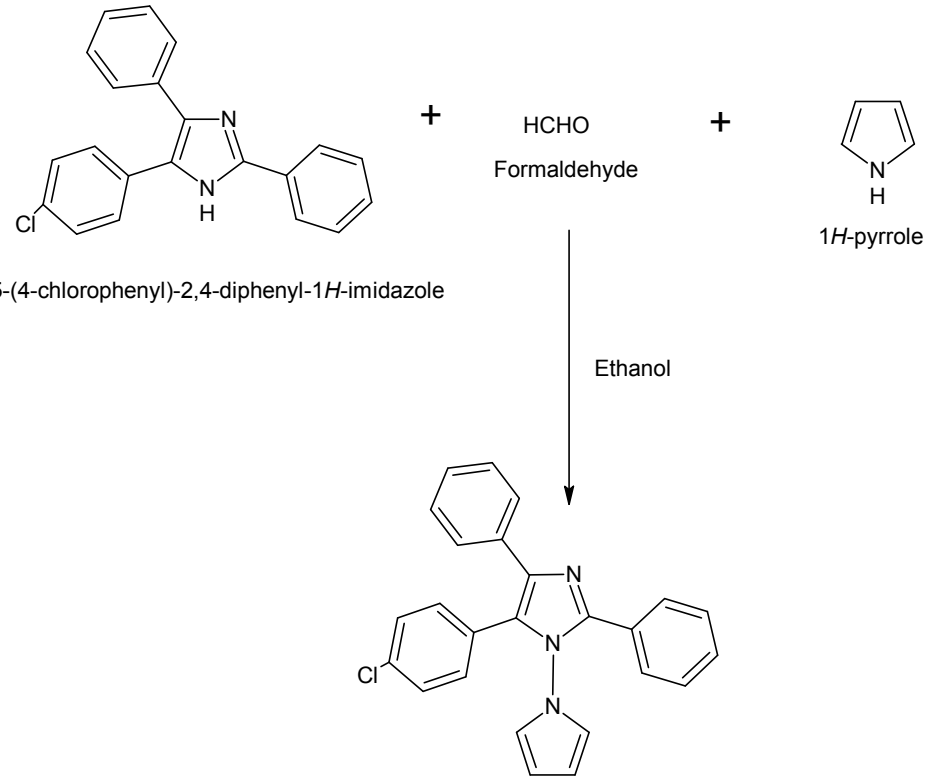
CHEMICALS REQURIED:

5-(4-Chlorophenyl)	-2,4-
diphenyl- 1H- imidazole	- 0.01M
Formaldehyde	- 3gm
Ethanol in pyrrole	- 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of pyrrole the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND A6



5-(4-chlorophenyl)-2,4-diphenyl-1*H*-imidazole

5-(4-chlorophenyl)-2,4-diphenyl-1-(1*H*-pyrrol-1-yl)-1*H*-imidazole

Molecular Formula	= $C_{25}H_{18}ClN_3$
Formula Weight	= 395.88352
Composition	= C(75.85%) H(4.58%) Cl(8.96%) N(10.61%)
Molar Refractivity	= 120.58 ± 0.5 cm^3
Molar Volume	= 327.8 ± 7.0 cm^3
Parachor	= 862.4 ± 8.0 cm^3
Index of Refraction	= 1.656 ± 0.05
Surface Tension	= 47.8 ± 7.0 dyne/cm
Density	= 1.20 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 47.80 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 395.118925 Da
Nominal Mass	= 395 Da
Average Mass	= 395.8835 Da

COMPOUND A7

Synthesis of 5-(4-chlorophenyl)2,4, Diphenyl -1H imidazole 1-yl piperzine

CHEMICALS REQUIRED:

5-(4-Chlorophenyl)-2,4-

diphenyl- 1H- imidazole - 0.01M

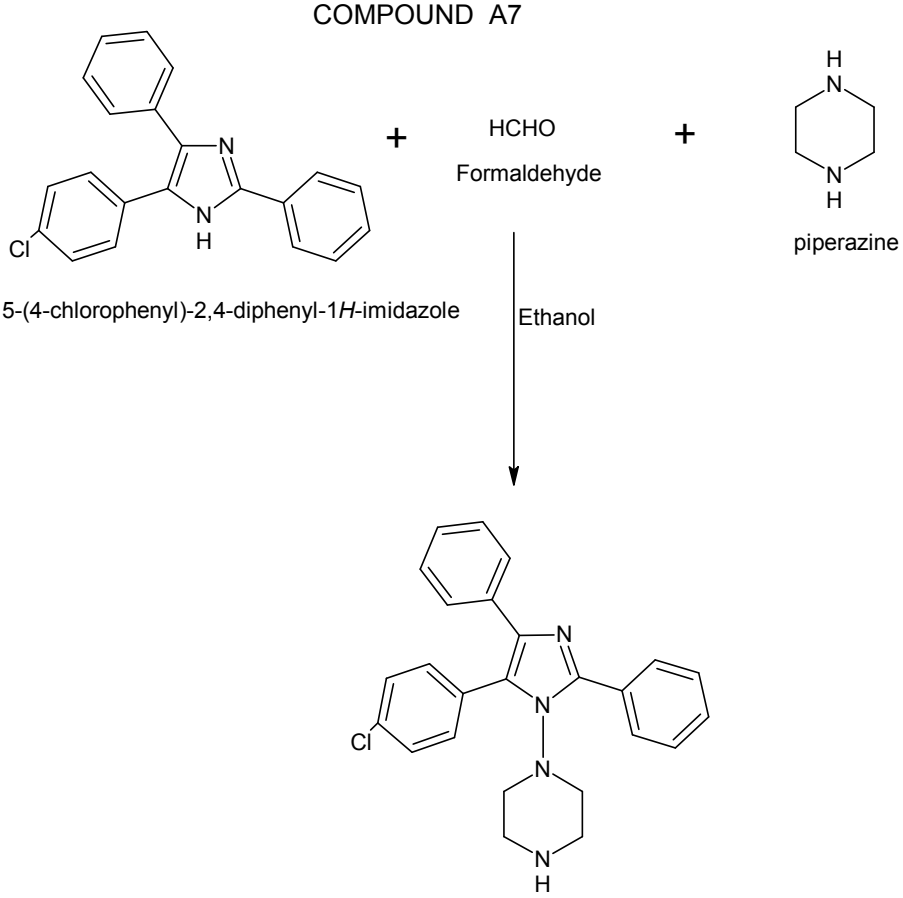
Formaldehyde - 3gm

Ethanol in piperzine - 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of piperzine the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND A7



5-(4-chlorophenyl)-2,4-diphenyl-1*H*-imidazole

5-(4-chlorophenyl)-2,4-diphenyl -1Himidazole -1-yl piperzine

Molecular Formula	= $C_{25}H_{23}ClN_4$
Formula Weight	= 414.92992
Composition	= C(72.37%) H(5.59%) Cl(8.54%) N(13.50%)
Molar Refractivity	= 123.64 ± 0.5 cm^3
Molar Volume	= 332.5 ± 7.0 cm^3
Parachor	= 882.2 ± 8.0 cm^3
Index of Refraction	= 1.666 ± 0.05
Surface Tension	= 49.5 ± 7.0 dyne/cm
Density	= 1.24 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 49.01 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 414.161124 Da
Nominal Mass	= 414 Da
Average Mass	= 414.9299 Da

COMPOUND A8

Synthesis of 5- (4-Chlorophenyl) N,N diphenyl-1H-imidazol amine

CHEMICALS REQUIRED:

5-(4-Chlorophenyl)-2,4-

diphenyl- 1H- imidazole - 0.01M

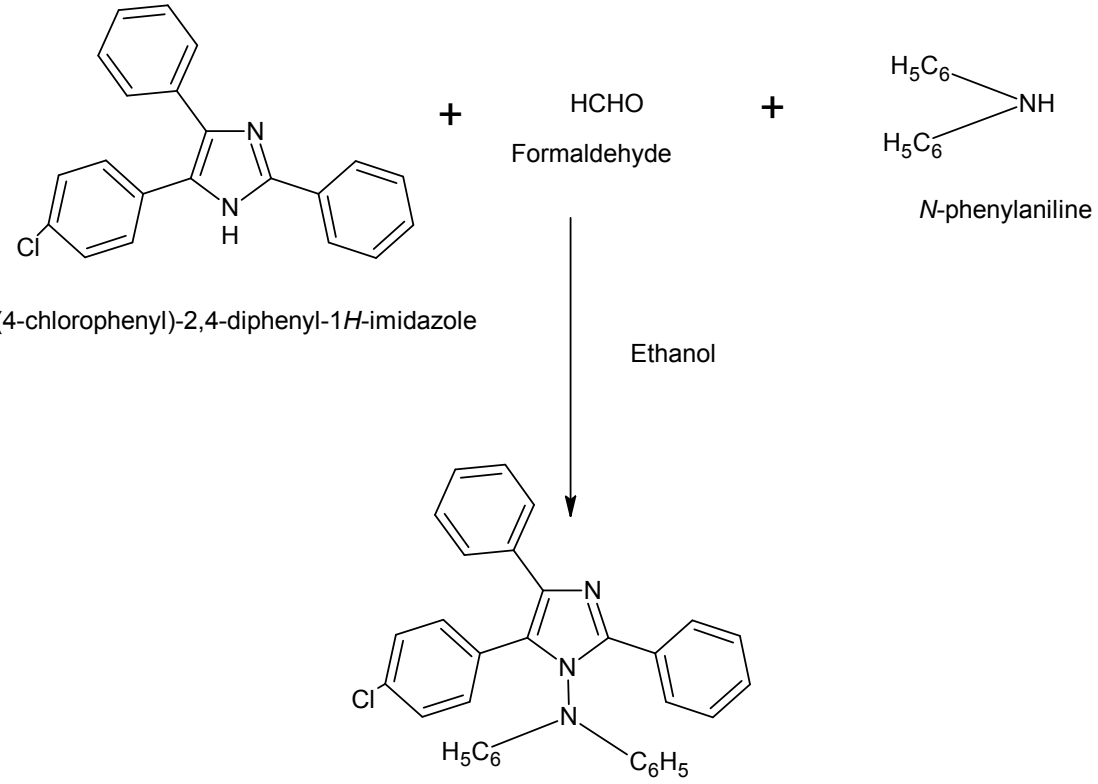
Formaldehyde - 3gm

Ethanol in diphenyl amine - 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of diphenyl amine the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND A8



5-(4-chlorophenyl)-2,4-diphenyl-1*H*-imidazole

5 -(4 -chlorophenyl)N,N diphenyl 2,4 diphenyl - 1H - imidazol amine

Molecular Formula	= $C_{33}H_{24}ClN_3$
Formula Weight	= 498.01676
Composition	= C(79.59%) H(4.86%) Cl(7.12%) N(8.44%)
Molar Refractivity	= 154.90 ± 0.5 cm^3
Molar Volume	= 427.6 ± 7.0 cm^3
Parachor	= 1116.5 ± 8.0 cm^3
Index of Refraction	= 1.644 ± 0.05
Surface Tension	= 46.4 ± 7.0 dyne/cm
Density	= 1.16 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 61.41 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 497.165875 Da
Nominal Mass	= 497 Da
Average Mass	= 498.0168

COMPOUND A9

Synthesis of 5-(4-chlorophenyl) 2,4diphenyl -1-(pyrrolidin - 1-yl)-1H- imidazole

CHEMICALS REQUIRED:

5-(4-Chlorophenyl)-2,4-

diphenyl- 1H- imidazole - 0.01M

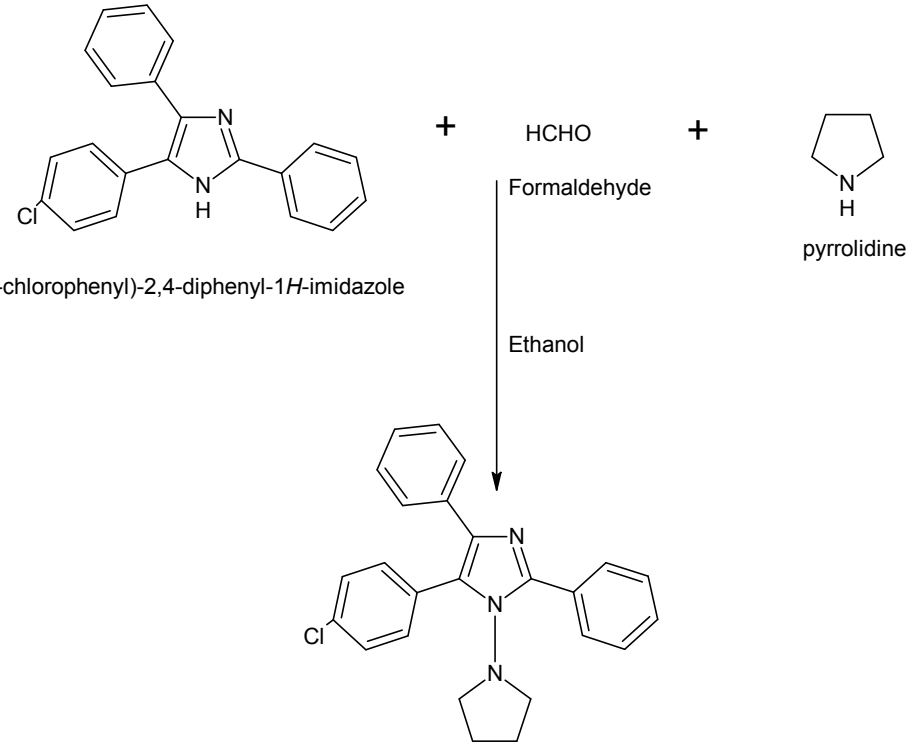
Formaldehyde - 3gm

Ethanol in pyrrolidine - 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of pyrrolidine the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND A9



5-(4-chlorophenyl)-2,4-diphenyl-1*H*-imidazole

5 -(4 -chlorophenyl) 2,4 diphenyl -1 -(pyrrolidin - 1 - yl) - 1H - imidazole

Molecular Formula	= $C_{25}H_{22}ClN_3$
Formula Weight	= 399.91528
Composition	= C(75.08%) H(5.54%) Cl(8.87%) N(10.51%)
Molar Refractivity	= 120.58 ± 0.5 cm^3
Molar Volume	= 327.8 ± 7.0 cm^3
Parachor	= 862.4 ± 8.0 cm^3
Index of Refraction	= 1.656 ± 0.05
Surface Tension	= 47.8 ± 7.0 dyne/cm
Density	= 1.21 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 47.80 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 399.150225 Da
Nominal Mass	= 399 Da
Average Mass	= 399.9153 Da

COMPOUND A10

Synthesis of 5-(4-chlorophenyl)- N,N-dimethyl 2,4 diphenyl- 1H-imidazol-1-amine

CHEMICALS REQUIRED:

5-(4-Chlorophenyl)-2,4-

diphenyl- 1H- imidazole - 0.01M

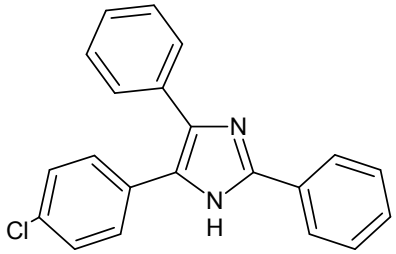
Formaldehyde - 3gm

Ethanol in dimethyl amin - 10%

PROCEDURE:

The mixture of ethanolic solution of 0.01M compound and formaldehyde 3gm was added slowly to ethanolic solution of dimethyl amine the reaction mixture is stirred more than one hour at room temperature and kept it over night in a refrigerator the solid form is filtered and is washed with ethanol.

COMPOUND A10



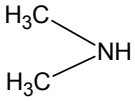
5-(4-chlorophenyl)-2,4-diphenyl-1*H*-imidazole

\+

HCHO

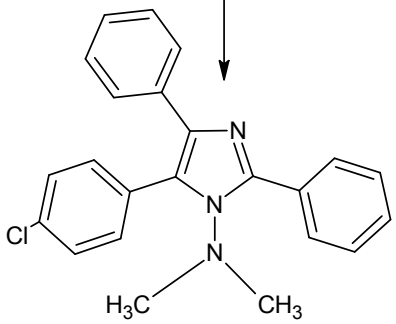
Formaldehyde

\+



N-methylmethanamine

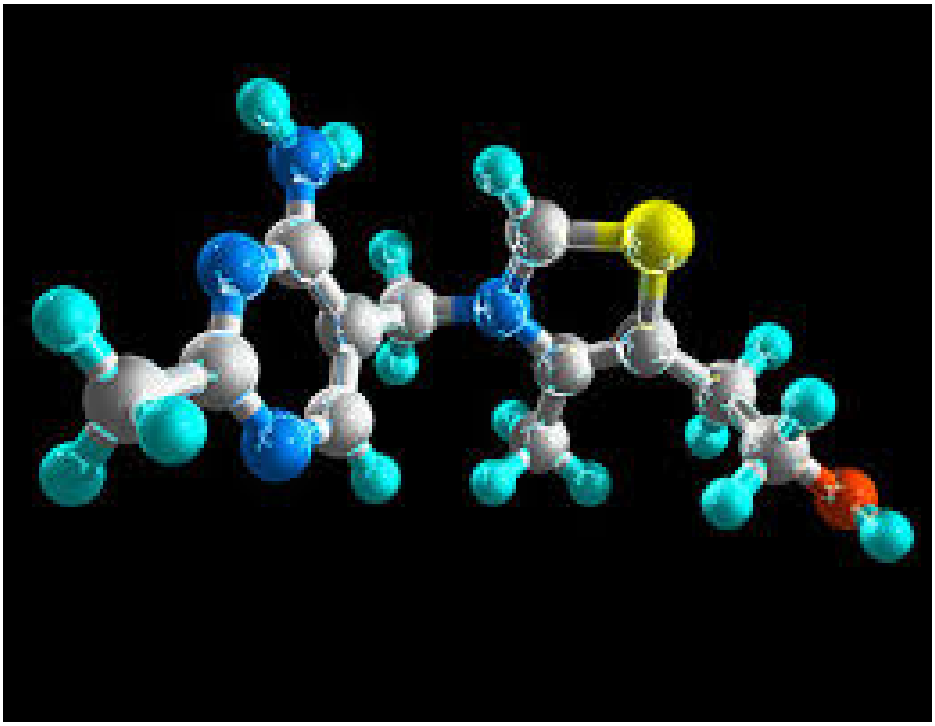
Ethanol



5-(4-chlorophenyl)-*N*,*N*-dimethyl-2,4-diphenyl-1*H*-imidazol-1-amine

Molecular Formula	= $C_{23}H_{20}ClN_3$
Formula Weight	= 373.878
Composition	= C(73.89%) H(5.39%) Cl(9.48%) N(11.24%)
Molar Refractivity	= 113.54 ± 0.5 cm^3
Molar Volume	= 322.5 ± 7.0 cm^3
Parachor	= 825.0 ± 8.0 cm^3
Index of Refraction	= 1.621 ± 0.05
Surface Tension	= 42.8 ± 7.0 dyne/cm
Density	= 1.15 ± 0.1 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 45.01 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 373.134575 Da
Nominal Mass	= 373 Da
Average Mass	= 373.878 Da

MOLECULAR DESGIN

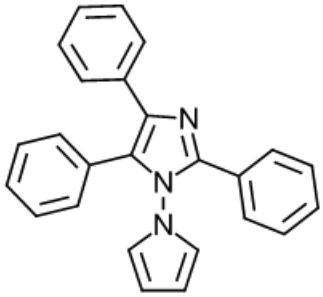


MOLECULAR DESIGN

CHEMDOODLE

COMPOUND A1

2,4,5triphenyl -1-(1H-pyrrol-1-yl) -1H- imidazole



Molecular Formula = $C_{25}H_{19}N_3$

Molecular Mass = 361.4384 u

Hydrogen Bond Donor Count = 0

Hydrogen Bond Acceptor Count = 0

T_f = 452.8900 K

T_b = 915.3601 K

CMR = 113.8130 cm³/mol

AMR = 113.7630 cm³/mol

XlogP v2.0 = 6.2320

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

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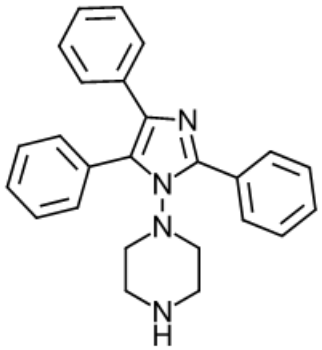
COMPOUND A2

2,4,5triphenyl -1-(1H-piperzine-1-yl) -1H- imidazole



Molecular Formula = $C_{25}H_{24}N_4$

Molecular Mass = 380.4848 u

Hydrogen Bond Acceptor Count = 2

Hydrogen Bond Donor Count = 1

CMR = 118.5580 cm^3/mol

AMR = 119.3557 cm^3/mol

T_b = 957.2101 K

T_f = 515.7101 K

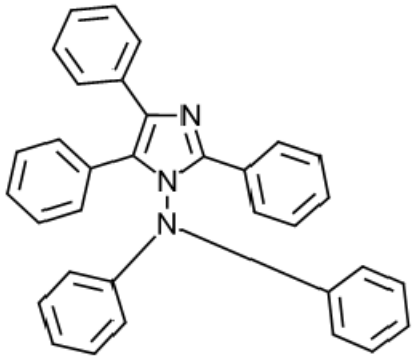
XlogP v2.0 = 5.8520

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

COMPOUND A3

N,N diphenyl-2,4,5 triphenyl -1H- Imidazole- 1- amine



Molecular Formula = $C_{33}H_{25}N_3$

Molecular Mass = 463.5717 u

Hydrogen Bond Donor Count = 0

Hydrogen Bond Acceptor Count = 1

T_b = 1113.4003 K

T_f = 527.5502 K

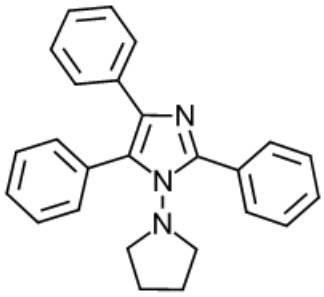
XlogP v2.0 = 8.143

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

COMPOUND A4

2,4,5triphenyl -1-(1H-pyrrolidin-1-yl) -1H-Imidazole



Molecular Formula = $C_{25}H_{23}N_3$

Molecular Mass = 365.4702 u

Hydrogen Bond Acceptor Count = 1

Hydrogen Bond Donor Count = 0

T_f = 463.0501 K

T_b = 907.0401 K

AMR = 115.7200 cm^3/mol

CMR = 114.8710 cm^3/mol

XlogP v2.0 = 6.2940

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

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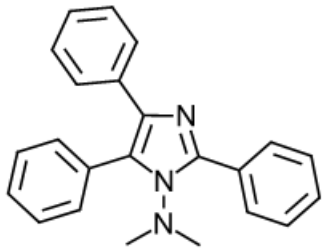
COMPOUND A5

N,N dimethyl 2,4,5 triphenyl-1H- Imidazol - amine



Molecular Formula = $C_{23}H_{21}N_3$

Molecular Mass = 339.4329 u

Hydrogen Bond Donor Count = 0

Hydrogen Bond Acceptor Count = 1

T_f = 407.7700 K

T_b = 862.6801 K

CMR = 107.3690 cm³/mol

AMR = 108.6000 cm³/mol

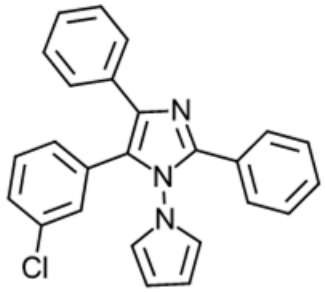
XlogP v2.0 = 5.0110

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

C0MPOUND A6

5-[4- chlorophenyl2,4, diphenyl -1-(1H-pyrrol-1-yl) -1H- imidazole



Molecular Formula = $C_{25}H_{18}ClN_3$

Molecular Mass = 395.8835 u

Hydrogen Bond Acceptor Count = 0

Hydrogen Bond Donor Count = 0

T_f = 468.8500 K

T_b = 952.6701 K

CMR = 118.7270 cm^3/mol

AMR = 118.7730 cm^3/mol

XlogP v2.0 = 6.8540

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

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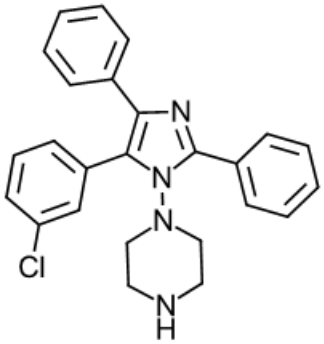
COMPOUND A7

5-(4-chlorophenyl)2,4, Diphenyl -1H imidazole 1-yl piperzine



Molecular Formula = $C_{25}H_{23}ClN_4$

Molecular Mass = 414.9299 u

Hydrogen Bond Acceptor Count = 2

Hydrogen Bond Donor Count = 1

T_f = 531.6701 K

T_b = 994.5201 K

CMR = 123.4720 cm³/mol

AMR = 124.3657 cm³/mol

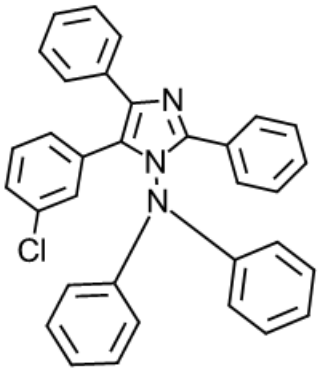
Bioavailability Score = 0.1700

XlogP v2.0 = 6.4740

Lipinski's Rule of 5 Violations Count = 1

COMPOUND A8

5- (4-Chlorophenyl) N,N diphenyl-1H-imidazol amine



Molecular Formula = $C_{33}H_{24}ClN_3$

Molecular Mass = 498.0168 u

Hydrogen Bond Donor Count = 0

Hydrogen Bond Acceptor Count = 1

T_f = 543.5101 K

T_b = 1150.7102 K

CMR = 153.2310 cm³/mol

AMR = 153.9661 cm³/mol

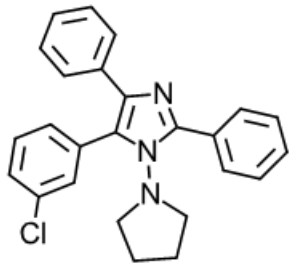
XlogP v2.0 = 8.7650

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

COMPOUND A9

5-(4-chlorophenyl) 2,4diphenyl -1-(pyrrolidin - 1-yl)-1H- imidazole



Molecular Formula = $C_{25}H_{22}ClN_3$

Molecular Mass = 399.9152 u

Hydrogen Bond Donor Count = 0

Hydrogen Bond Acceptor Count = 1

T_f = 479.0101 K

T_b = 944.3501 K

CMR = 119.7850 cm³/mol

AMR = 120.7300 cm³/mol

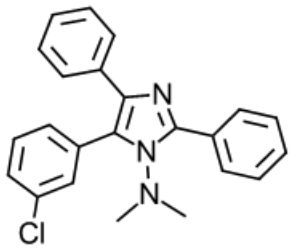
XlogP v2.0 = 6.9160

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

COMPOUND A10

5-(4-chlorophenyl)- N,N-dimethyl 2,4 diphenyl- 1H-imidazol-1-amine



Molecular Formula = $C_{23}H_{20}ClN_3$

Molecular Mass = 373.8780 u

Hydrogen Bond Donor Count = 0

Hydrogen Bond Acceptor Count = 1

T_f = 423.7300 K

T_b = 899.9901 K

CMR = 112.2830 cm^3/mol

AMR = 113.6100 cm^3/mol

XlogP v2.0 = 5.6330

Bioavailability Score = 0.1700

Lipinski's Rule of 5 Violations Count = 1

LIPINSKIS RULE BY CHEMDOODLE

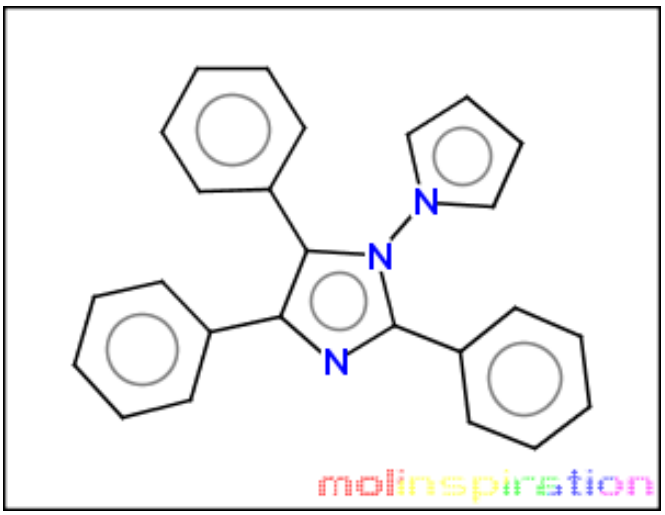
Table.No:1

Code	M.W	M.R cm^3/mol	H bond acceptor	H bond donor	Log P	No.of.criteria
Rule	**<500**	**<150**	**<10**	**<5**	**<5**	**Atleast 3**
A1	361.4	113.8	0	0	6.2	4
A2	380.4	119.3	2	1	5.8	4
A3	463.5	150.3	1	0	8.1	4
A4	365.4	115.7	1	0	6.2	4
A5	339.4	108.6	1	0	5	4
A6	395.8	118.7	0	0	6.8	4
A7	414.9	123.4	2	1	6.4	4
A8	498	153.9	1	0	8.7	4
A9	399.9	120	1	0	6.9	4
A10	373.8	113.6	1	0	5.6	4

MOLINSPIRATION

Calculation of molecular properties and bioactivity score

COMPOUND A1



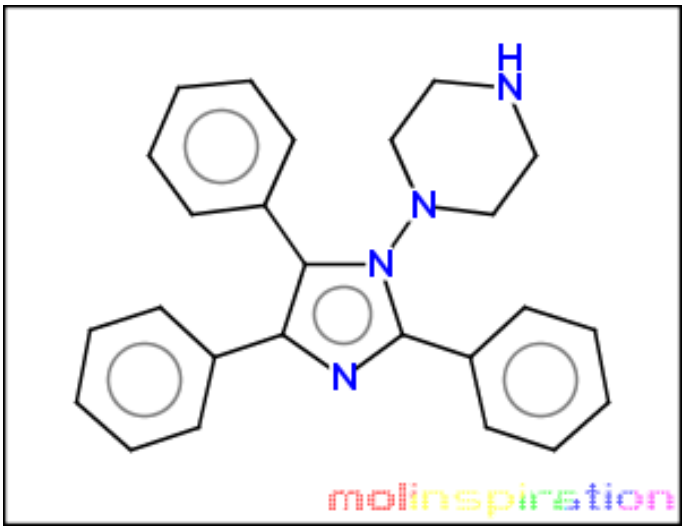
Molinspiration property engine v2013.09

miLogP	6.038
TPSA	22.76
natoms	28.0
MW	361.448
nON	3
nOHNH	0
nviolations	1
nrotb	4
volume	336.256

Molinspiration bioactivity score v2011.06

GPCR ligand	-0.12
Ion channel modulator	-0.13
Kinase inhibitor	0.03
Nuclear receptor ligand	-0.22
Protease inhibitor	-0.41
Enzymeinhibitor	-0.09

COMPOUND A2



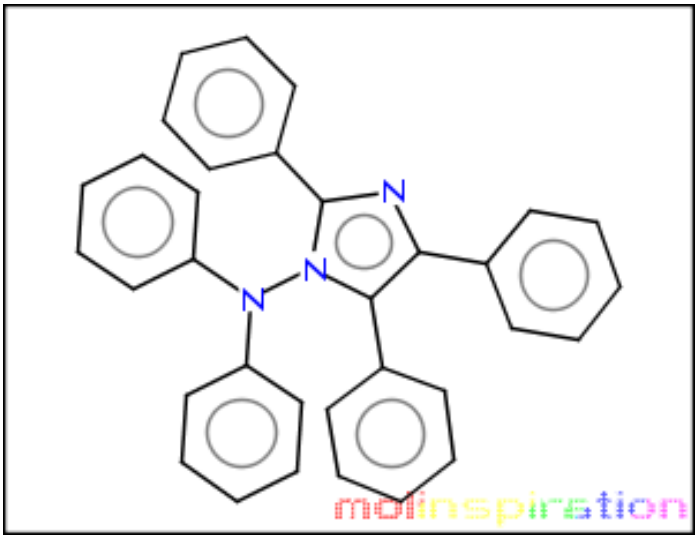
Molinspiration property engine v2013.09

miLogP	4.756
TPSA	33.091
natoms	29.0
MW	380.495
nON	4
nOHNH	1
nviolations	0
nrotb	4
volume	361.032

Molinspiration bioactivity score v2011.06

GPCR ligand	0.20
Ion channel modulator	-0.02
Kinase inhibitor	0.15
Nuclear receptor ligand	-0.14
Protease inhibitor	-0.20
Enzymeinhibitor	0.14

COMPOUND A3



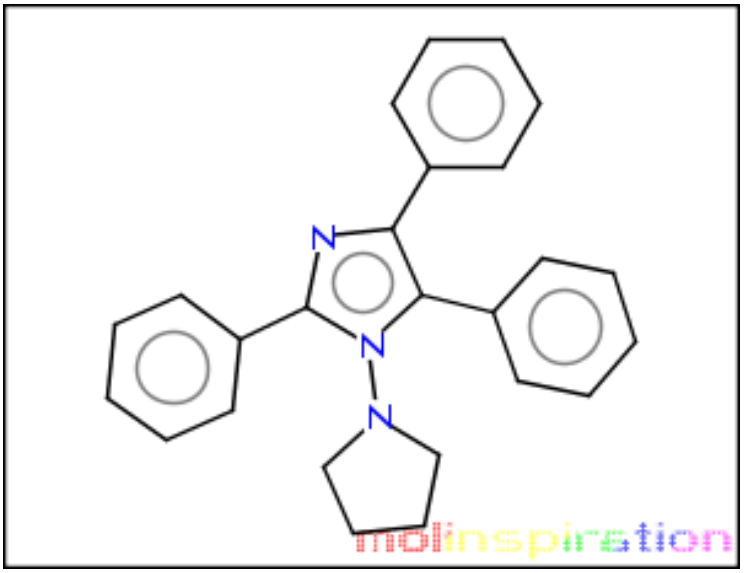
Molinspiration property engine v2013.09

miLogP	8.618
TPSA	21.064
natoms	36.0
MW	463.584
nON	3
nOHNH	0
nviolations	1
nrotb	6
volume	435.081

Molinspiration bioactivity score v2011.06

GPCR ligand	-0.02
Ion channel modulator	-0.09
Kinase inhibitor	0.10
Nuclear receptor ligand	-0.07
Protease inhibitor	-0.24
Enzymeinhibitor	-0.00

COMPOUND A4



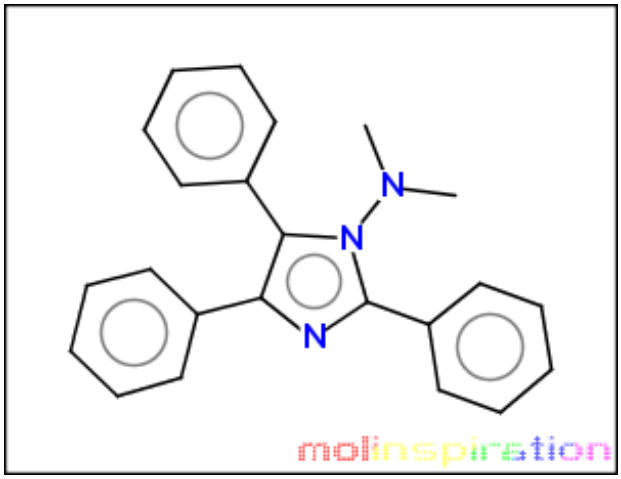
Molinspiration property engine v2013.09

miLogP	5.863
TPSA	21.064
natoms	28.0
MW	365.48
nON	3
nOHNH	0
nviolations	1
nrotb	4
volume	348.629

Molinspiration bioactivity score v2011.06

GPCR ligand	0.08
Ion channel modulator	-0.04
Kinase inhibitor	0.13
Nuclear receptor ligand	-0.08
Protease inhibitor	-0.21
Enzymeinhibitor	0.10

COMPOUND A5



Molinspiration property engine v2013.09

miLogP 5.46

TPSA 21.064

natoms 26.0

MW 339.442

nON 3

nOHNH 0

nviolations 1

nrotb 4

volume 325.386

Molinspiration bioactivity score v2011.06

GPCR ligand 0.02

Ion channel modulator -0.10

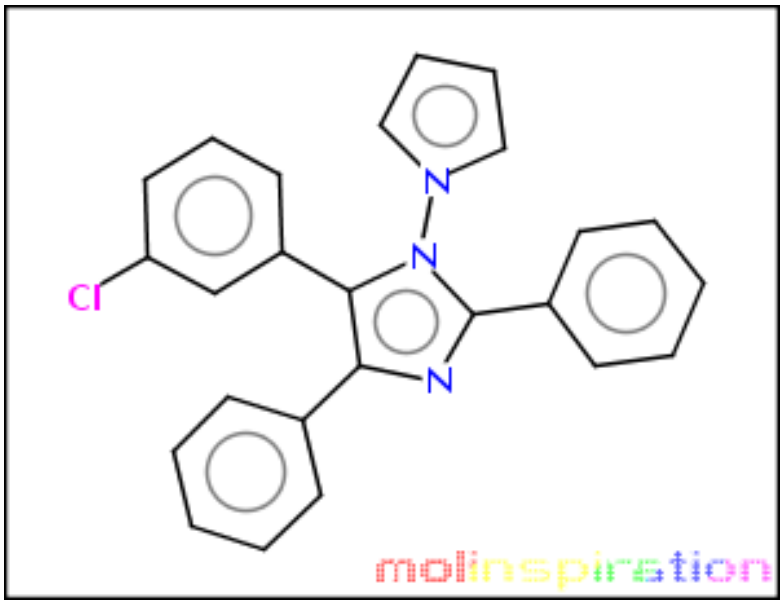
Kinase inhibitor 0.10

Nuclear receptor ligand -0.13

Protease inhibitor -0.21

Enzymeinhibitor 0.07

COMPOUND A6



Molinspiration property engine v2013.09

miLogP 6.692

TPSA 22.76

natoms 29.0

MW 395.893

nON 3

nOHNH 0

nviolations 1

nrotb 4

volume349.792

Molinspiration bioactivity scorev2011.06

GPCR ligand -0.12

Ion channel modulator -0.14

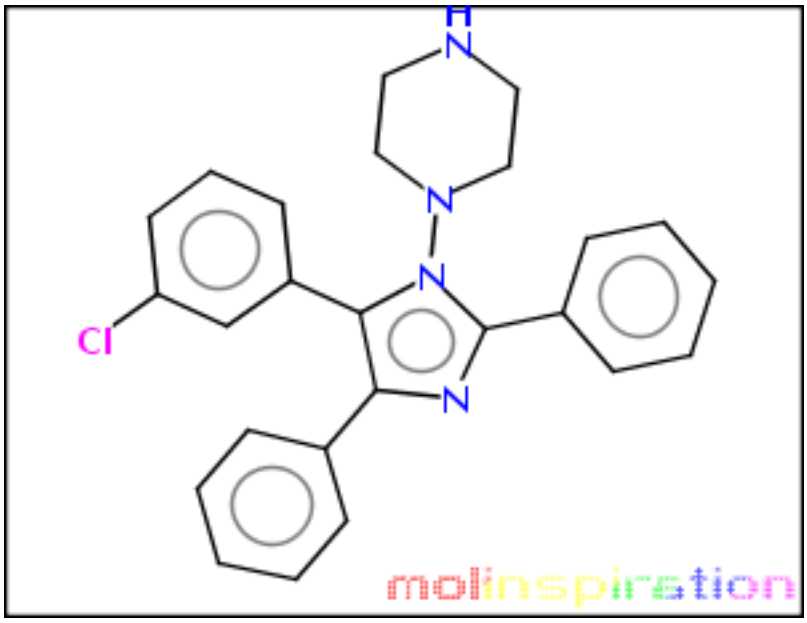
Kinasssse inhibitor 0.01

Nuclear receptor ligand -0.21

Protease inhibitor -0.45

Enzymeinhibitor -0.11

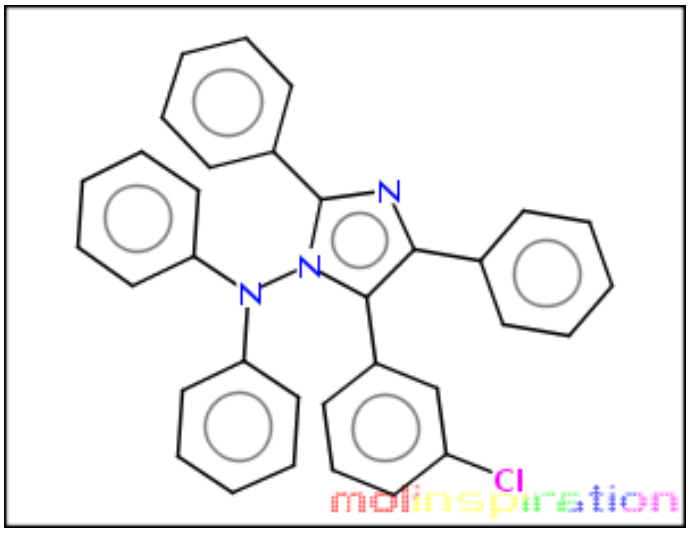
COMPOUND A7



Molinspiration property engine
v2013.09
miLogP 5.41
TPSA 33.091
natoms 30.0
MW 414.94
nON 4
nOHNH 1
nviolations 1
nrotb 4
volume 374.568

Molinspiration bioactivity score v2011.06
GPCR ligand 0.19
Ion channel modulator -0.04
Kinase inhibitor 0.13
Nuclear receptor ligand -0.13
Protease inhibitor -0.24
Enzymeinhibitor 0.11

COMPOUND A8



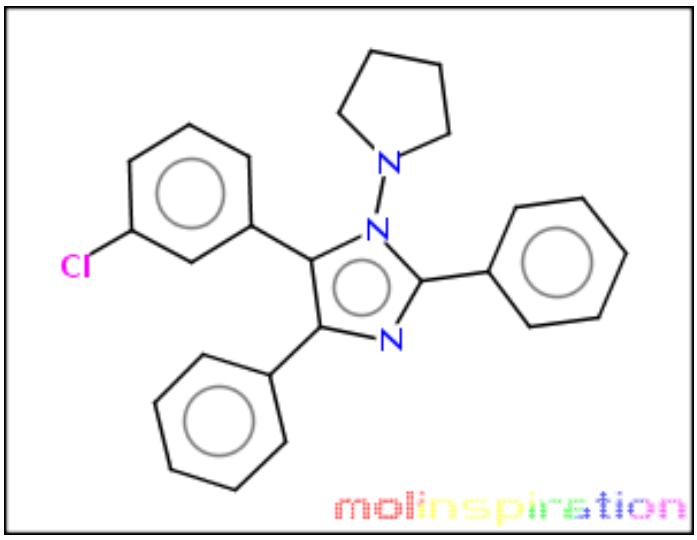
Molinspiration property engine v2013.09

miLogP	8.92
TPSA	21.064
natoms	37.0
MW	498.029
nON	3
nOHNH	0
nviolations	1
nrotb	6
volume	448.617

Molinspiration bioactivity score v2011.06

GPCR ligand	-0.02
Ion channel modulator	-0.13
Kinase inhibitor	0.09
Nuclear receptor ligand	-0.07
Protease inhibitor	-0.28
Enzymeinhibitor	-0.02S

COMPOUND A9



Molinspiration property engine v2013.09

miLogP 6.517

TPSA 21.064

natoms 29.0

MW 399.925

nON 3

nOHNH 0

nviolations 1

nrotb 4

volume 362.165

Molinspiration bioactivity score v2011.06

GPCR ligand 0.07

Ion channel modulator -0.06

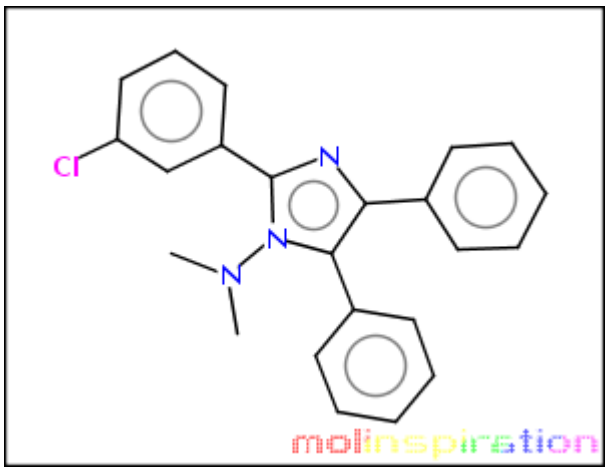
Kinase inhibitor 0.11

Nuclear receptor ligand -0.08

Protease inhibitor -0.26

Enzymeinhibitor 0.07

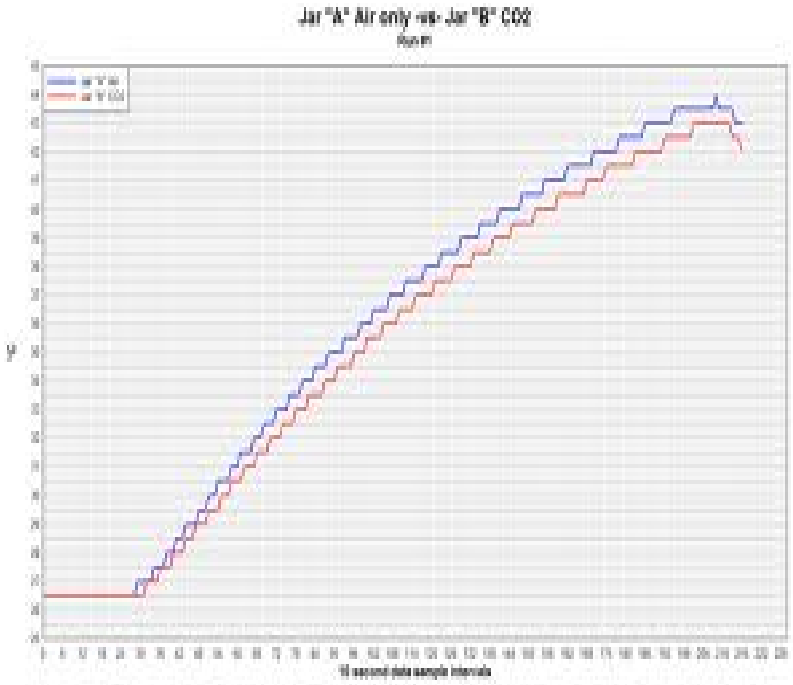
COMPOUND A10



Molinspiration property engine v2013.09

miLogP 6.114
TPSA 21.064
natoms 27.0
MW 373.887
nON 3
nOHNH 0
nviolations 1
nrotb 4
volume 338.922
Molinspiration bioactivity score v2011.06
GPCR ligand 0.02
Ion channel modulator -0.11
Kinase inhibitor 0.08
Nuclear receptor ligand -0.13
Protease inhibitor -0.26
Enzymeinhibitor 0.04

PHYSICAL DATA



PHYSICAL DATA OF SYNTHESIZED COMPOUNDS

Table.No:2

CODE	MOLECULAR FORMULA	MOLECULAR WEIGHT	I.U.P.A.C NAME
A1	C25H19N3	361.438	2,4,5 triphenyl-1-(1H-pyrrole-1-yl)-1H-imidazole
A2	C25H24 N4	380.484	2,4,5 triphenyl-1-(1H piperzine-1-yl) -1H-imidazole
A3	C33H25N3	463.57	N,N diphenyl-2,4,5triphenyl -1H-imidazol-1-amine
A4	C25H23N3	365.47	2,4,5 Triphenyl-1-(pyrrolidin-1-yl)-1H-imidazdazole
A5	C23H21N3	339.43	N,N dimethyl-2,4,5,triphenyl -1H-imidazol-1-amine
A6	C25H18ClN3	395.88	5-(4-Chlorophenyl)-2,4-diphenyl-1-(1H-pyrrole-1-yl)-1H-imidazole
A7	C25H23ClN4	414.92	5-(4-Chlorophenyl)-2,4-diphenyl-1H imidazole-1-yl piperzine
A8	C33H24ClN3	498.016	5-(4-chlorophenyl)N,N-diphenyl 2,4 diphenyl-1H-imidazol amine
A9	C25H22ClN3	399.91	5-(4-chlorophenyl) 2,4 diphenyl-1-(pyrrolidin-1-yl)-1H-imidazole
A10	C23H20ClN3	373.87	5-(4-chlorophenyl)-N,N-methyl-2,4diphenyl-1H-imidazol-1-amine

MELTING POINT

Table.No:3

COMPOUND	APPEARANCE	%YIELD	MELTING POINT -◦C	SOLUBILITY
A1	Brown solid	78	130	DMSO
A2	Sandal solid	72	110	DMSO
A3	White solid	75	125	DMSO
A4	White solid	77	140	DMSO
A5	Pale white solid	74	120	DMSO
A6	Dark brown solid	79	135	DMSO
A7	Pale orange solid	70	120	DMSO
A8	Pale yellow solid	68	100	DMSO
A9	White solid	71	130	DMSO
A10	Pale white solid	76	105	DMSO

THIN LAYER CHROMATOGRAPHY[21]

The thin layer chromatography was used to determine the purity of the compounds in readymade silica gel plate and spots were visualized using iodine chamber.

SOLVENT SYSTEM USED:

HEXANE : ETHYL ACETATE

1 : 1

Table.No:4

S.NO	COMPOUND	Rf VALUE
1	A1	0.64
2	A2	0.72
3	A3	0.85
4	A4	0.61
5	A5	0.78
6	A6	0.61
7	A7	0.75
8	A8	0.83
9	A9	0.66
10	A10	0.80

ELEMENTAL COMPOSITION ANALYSIS

Table.No.5

COMPOUND	C	H	N	Cl
	%FOUND			
	%CALCULATED			
A1	83.08	5.3	11.63	-
A2	78.92	6.36	14.73	-
A3	83.50	5.44	9.06	-
A4	82.16	6.34	11.5	-
A5	81.38	6.24	12.38	-
A6	75.85	4.58	10.6	8.96
A7	72.37	5.59	13	8.54
A8	79.59	4.86	8.44	7.12
A9	75.08	5.54	10.5	8.87
A10	73.89	5.39	11.24	9.48

SPECTRAL DATA

MATERIALS AND METHODS[45,46,48,49]

INFRARED SPECTROSCOPY:

- IR is concerned with study of absorption of infrared radiation, which results in vibrational transition.
- Instrument – Shimadzhu FTIR
- Region 4000 - 400cm^{-1}
- Method - pressed pellet technique
- Values measured in cm^{-1}

1HNMR SPECTROSCOPY:

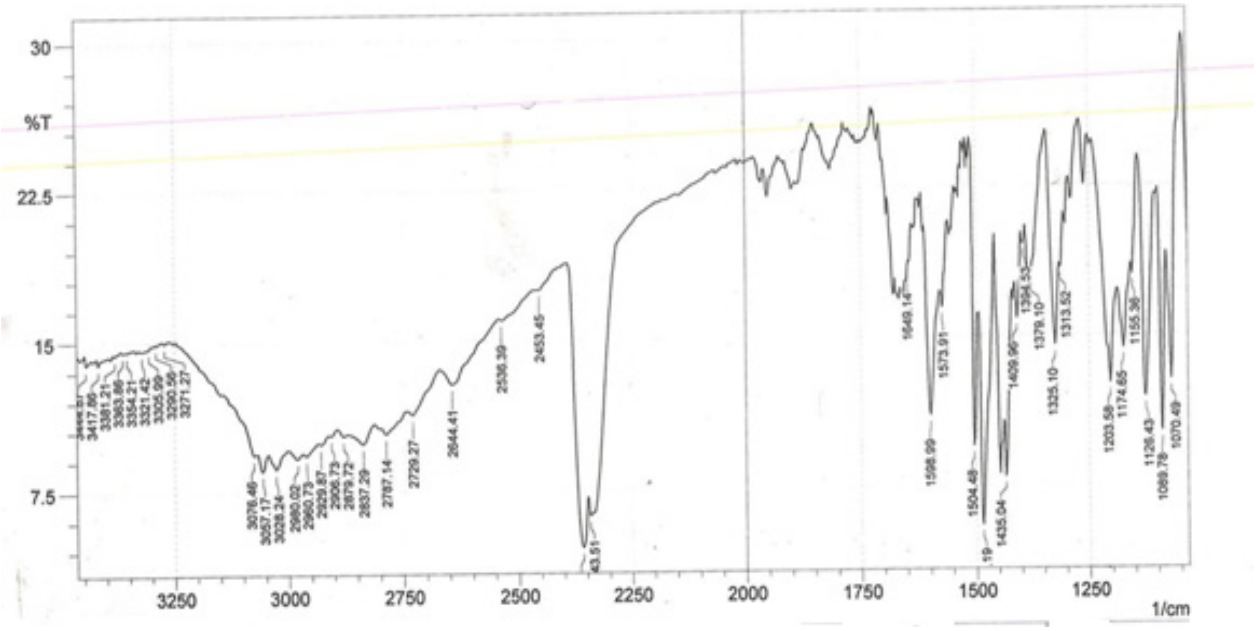
- NMR is the study of spin changes at the nuclear level when radio frequency energy is absorbed in the presence of magnetic field.
- Instrument - BrukerAvance II 400 NMR
- Solvent used -DMSO
- Tetra Methyl Silane used as internal standard
- Values measured in delta ppm

MASS SPECTROSCOPY:

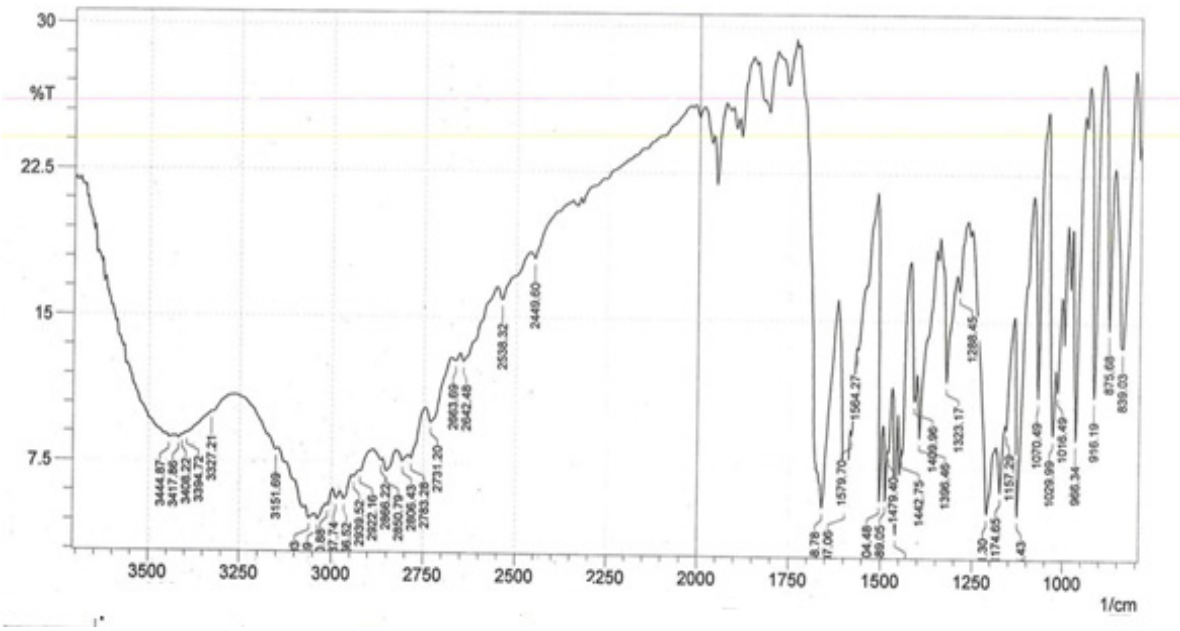
- It can be used to determine directly molecular weight
- The compound under investigation is bombared with a beam of electrons which produce an ionic molecule (or) ionic fragments of the original species
- The molecular ion is called as parent ion and it is designed as $M^{+\cdot}$
- The largest peak in the structure is called base peak.
- The molecular ion peak should have the largest m/e ratio.

INFRARED SPECTROSCOPY

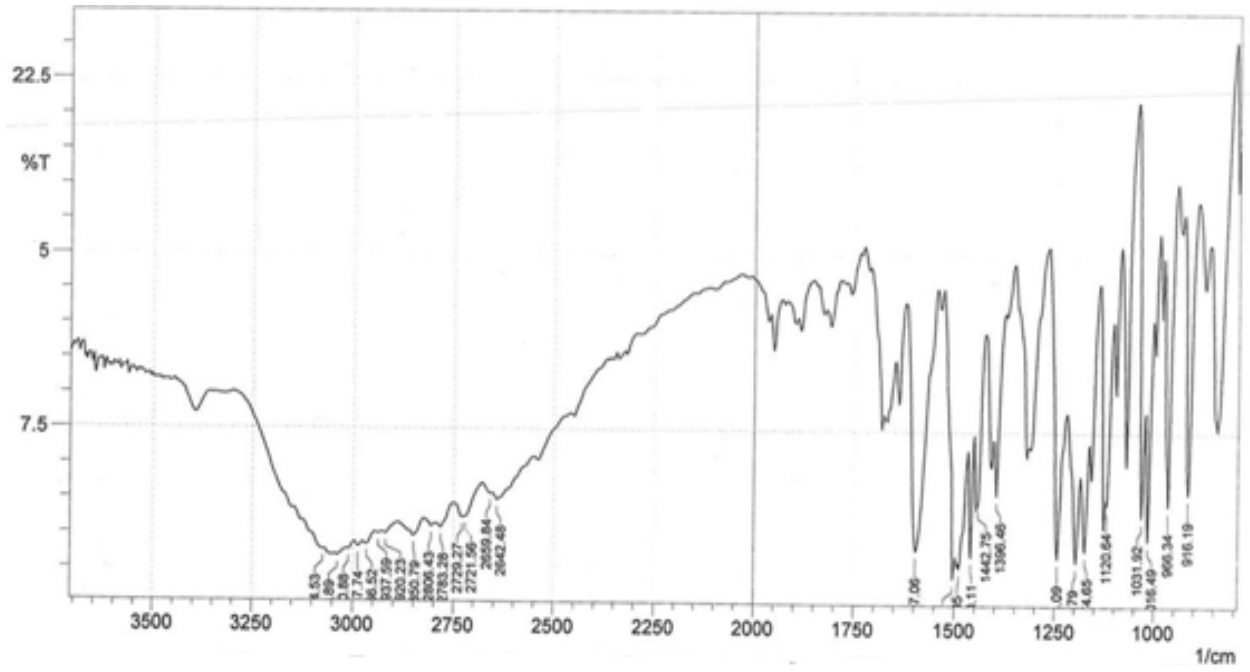
COMPOUND A1



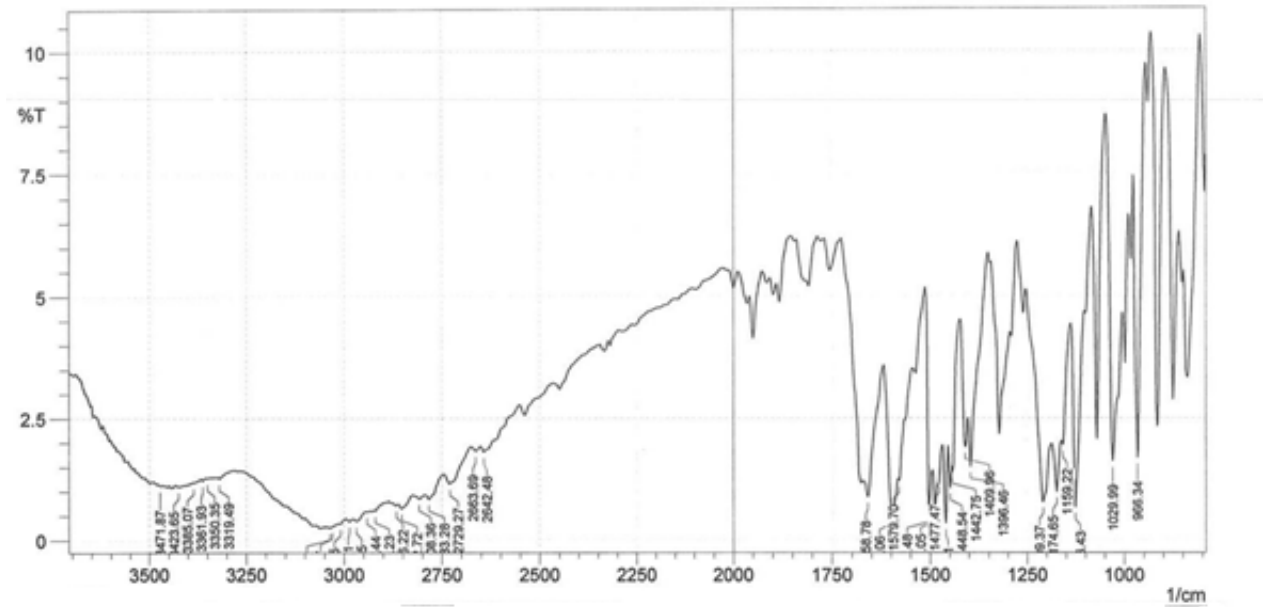
COMPOUND A2



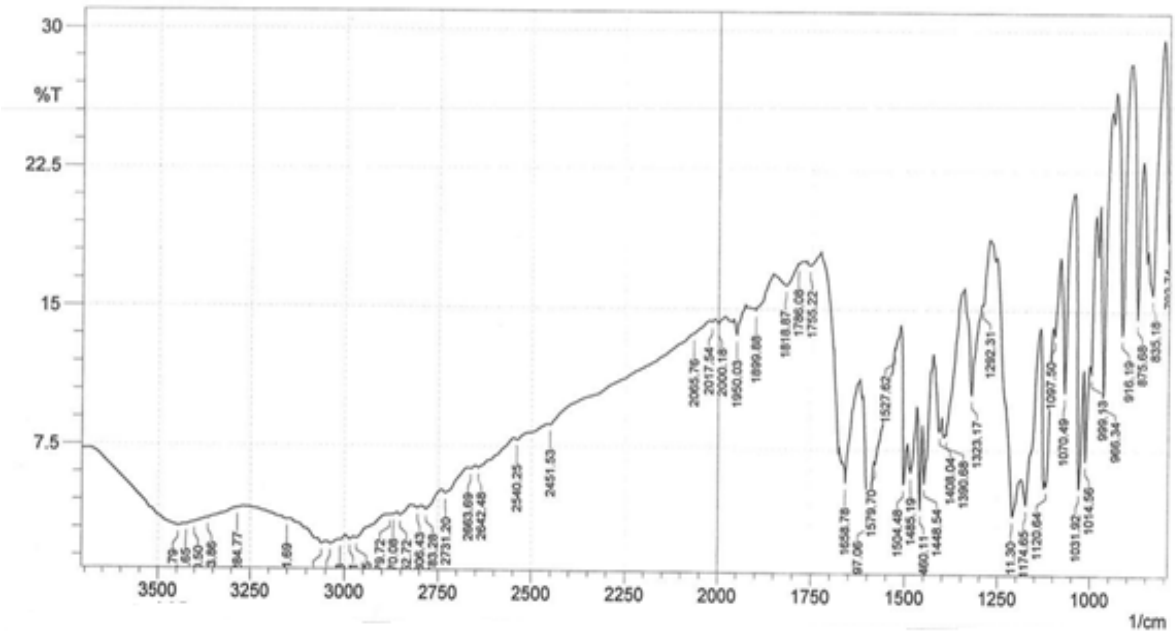
COMPOUND A3



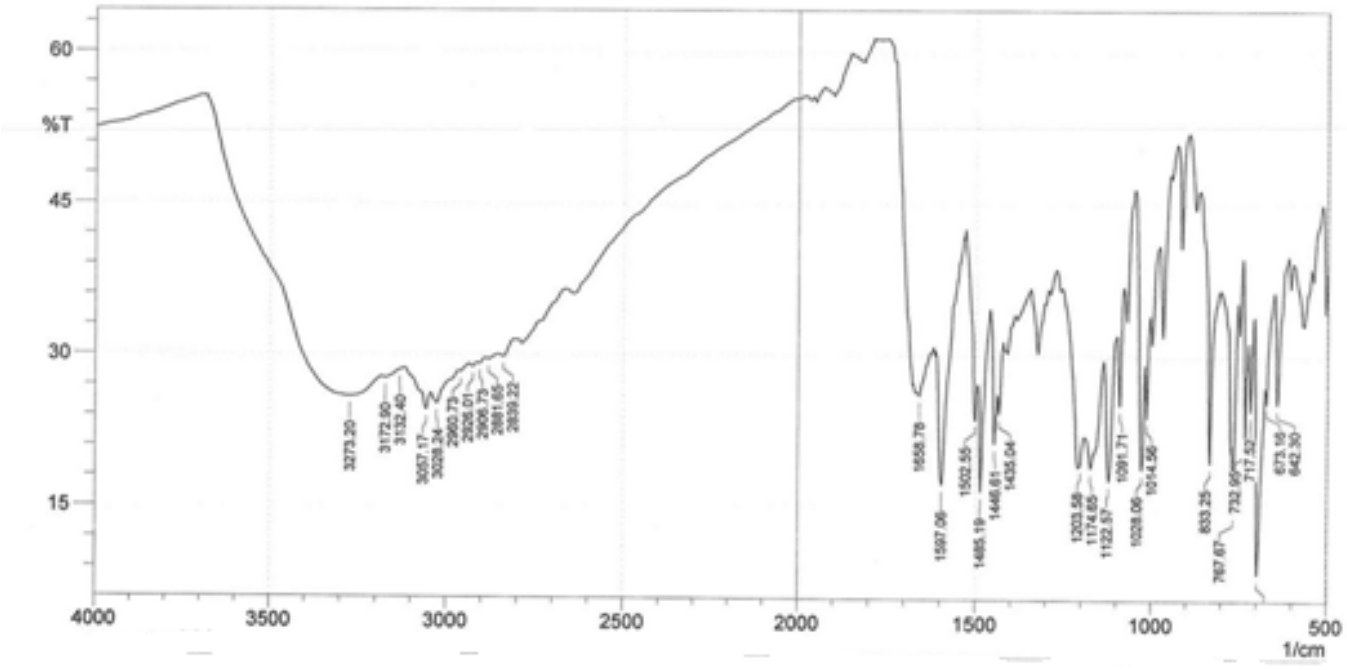
COMPOUND A4



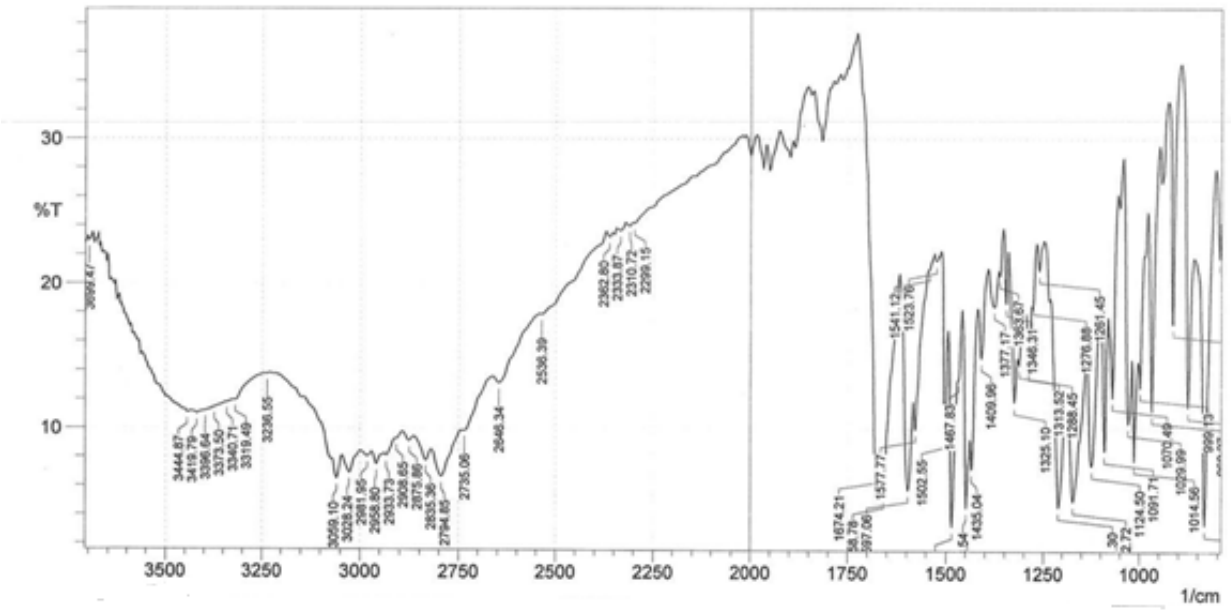
COMPOUND A5



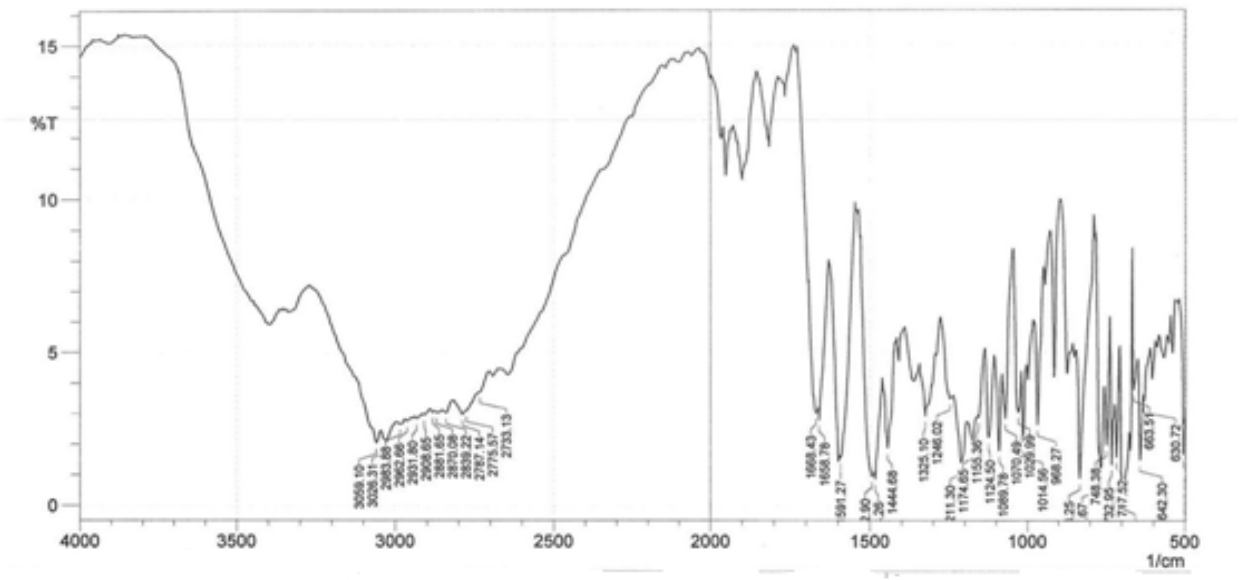
COMPOUND A6



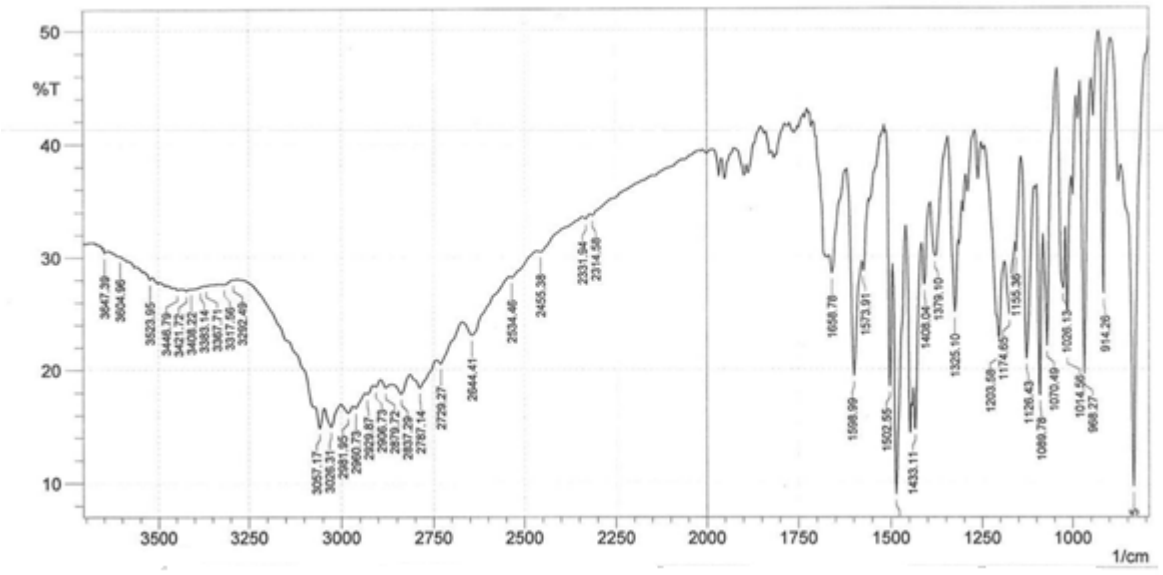
COMPOUND A7



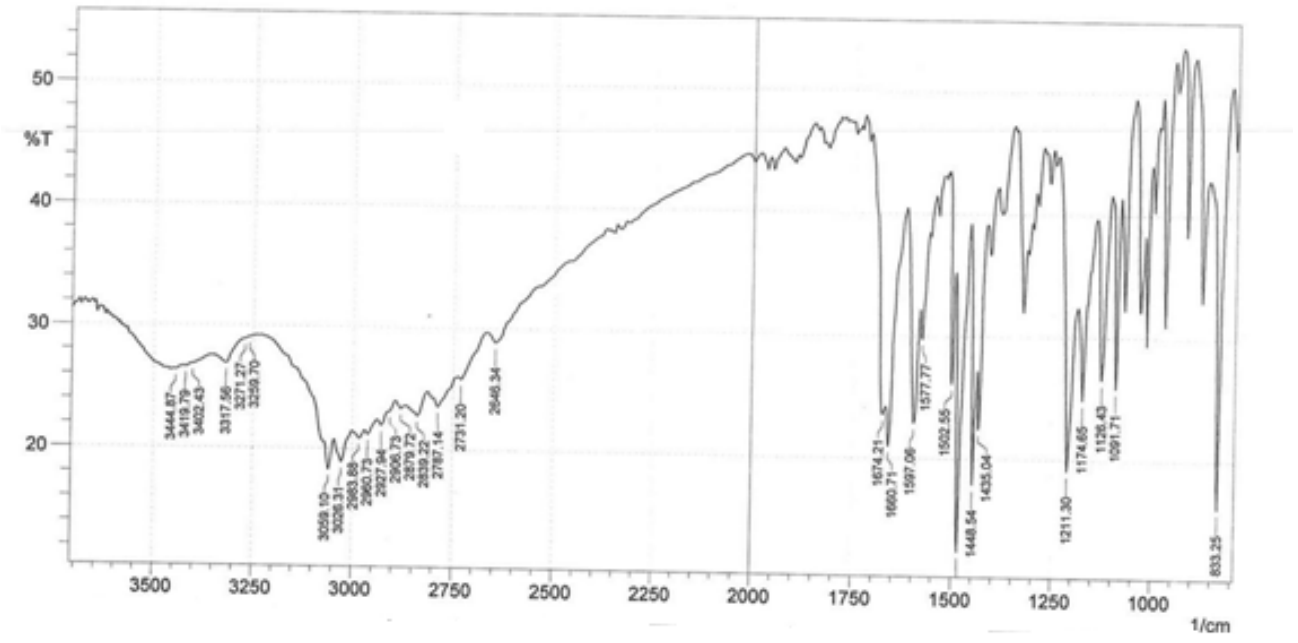
COMPOUND A8



COMPOUND A9



COMPOUND A10



INFRARED SPECTROSCOPY DATAS

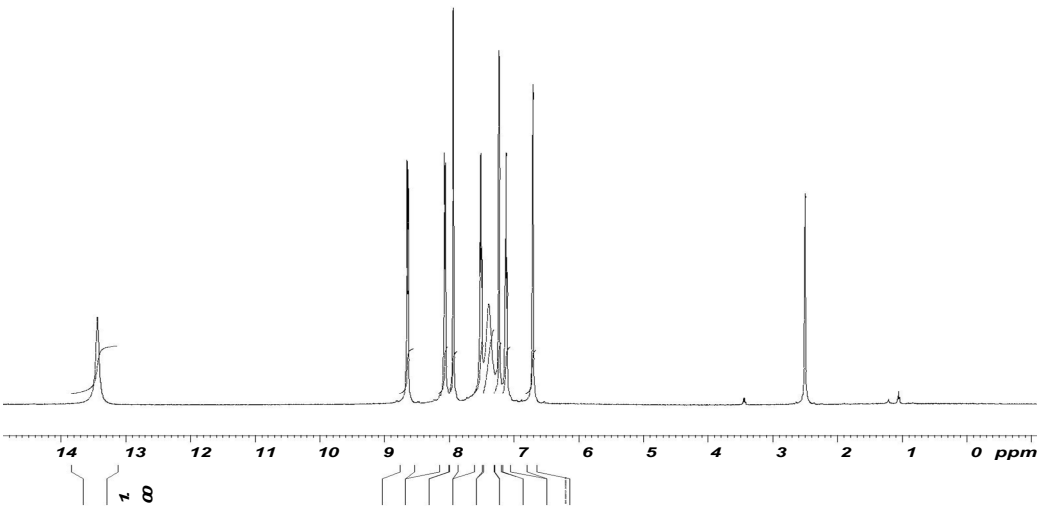
Table.No:6

CODE	TYPES OF VIBRATION	OBSERVED VALUE (cm^{-1})
A1	C=C str,in benzene	1598
	CH str aromatic	2960
	C – C str	1174
	C – N str	1325
	C = N str	1649
	N – H str	3028
	N – N str	3444
A2	C=C str,in benzene	1597
	CH str aromatic	2939
	C – C str	1174
	C – N str	1323
	C = N str	1658
	N – H str	3037
	N – N str	3444
A3	C=C str,in benzene	1597
	CH str aromatic	2920
	C – C str	1197
	C – N str	1244
	C = N str	1504
	N – H str	3010
	N – N str	3074
A4	C=C str,in benzene	1597
	CH str aromatic	2941
	C – C str	1174
	C – N str	1209
	C = N str	1658
	N – H str	3030
	N – N str	3471
A5	C=C str,in benzene	1597
	CH str aromatic	2879
	C – C str	1174
	C – N str	1323
	C = N str	1658
	N – H str	3037
	N – N str	3446

A6	C=C str,in benzene	1597
	CH str aromatic	2960
	C – C str	1174
	C – N str	1203
	C = N str	1658
	N – H str	3132
	N – N str	3273
	C – Clstr	767
A7	C=C str,in benzene	1597
	CH str aromatic	2958
	C – C str	1172
	C – N str	1346
	C = N str	1577
	N – H str	3028
	N – N str	3444
	C – Clstr	794
A8	C=C str,in benzene	1591
	CH str aromatic	2962
	C – C str	1174
	C – N str	1325
	C = N str	1668
	N – H str	3026
	N – N str	3059
	C – Clstr	767
A9	C=C str,in benzene	1598
	CH str aromatic	2960
	C – C str	1174
	C – N str	1325
	C = N str	1658
	N – H str	3026
	N – N str	3446
	C – Clstr	767
A10	C=C str,in benzene	1597
	CH str aromatic	2960
	C – C str	1174
	C – N str	1211
	C = N str	1674
	N – H str	3026
	N – N str	3444
	C – Clstr	767

1HNMR SPECTROSCOPY

COMPOUND A1

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Current Data Parameters
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EXPNO               11
PROCNO               1

F2 – Acquisition Parameters
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Time            22.10
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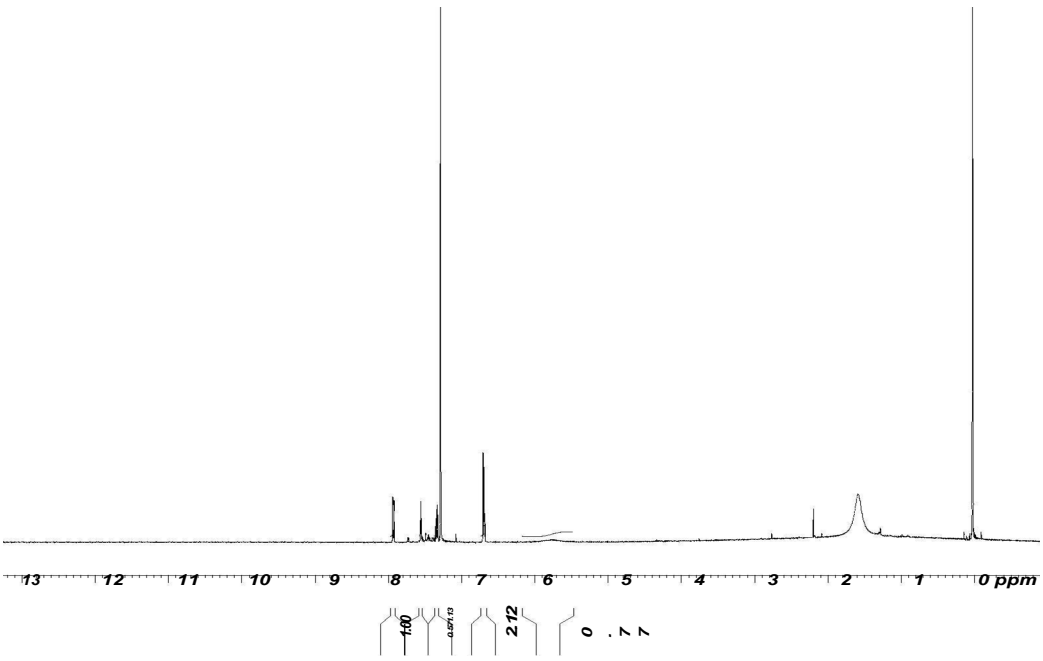
PROBHD    5 mm PABBO BB–
PULPROG          zg30
TD              32768
SOLVENT           DMSO
NS                 32
DS                  2
SWH          10330.578 Hz
FIDRES        0.315264 Hz
AQ           1.5860212 sec
RG                203
DW             48.400 usec
DE              6.50 usec
TE              300.1 K
D1          1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1               1H
P1             10.65 usec
PL1             0.00 dB
PL1W       23.53637505 W
SFO1        500.1330885 MHz

F2 – Processing parameters
SI              32768
SF         500.1300035 MHz
WDW                EM
SSB                 0
LB              0.30 Hz
GB                  0
PC              1.00
```

COMPOUND A2



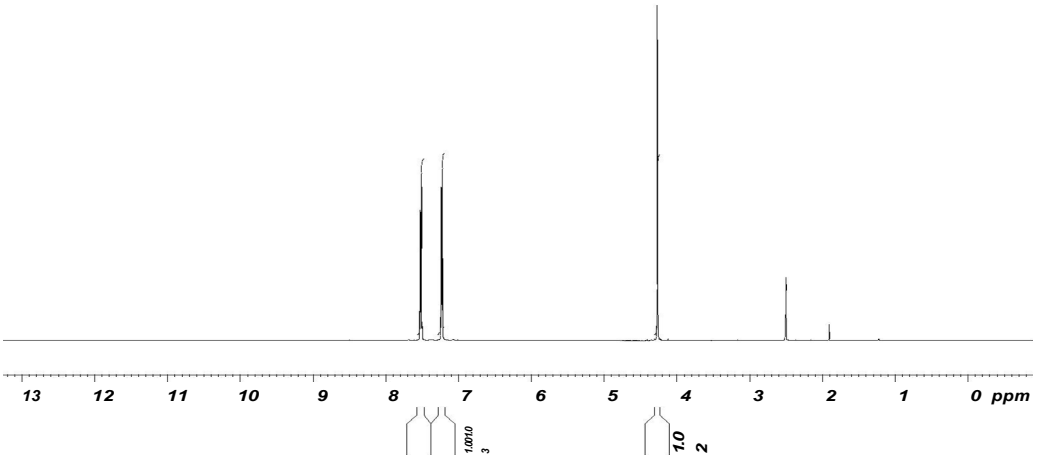

```
Current Data Parameters
NAME          Feb07–2014
EXPNO               27
PROCNO               1

F2 – Acquisition Parameters
Date_         20140207
Time            4.52
INSTRUM          spect
PROBHD    5 mm PABBO BB–
PULPROG          zg30
TD              32768
SOLVENT           DMSO
NS                 32
DS                  2
SWH          10330.578 Hz
FIDRES        0.315264 Hz
AQ           1.5860212 sec
RG                203
DW             48.400 usec
DE              6.50 usec
TE              299.3 K
D1          1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1               1H
P1             10.65 usec
PL1             0.00 dB
PL1W       23.53637505 W
SFO1        500.1330885 MHz

F2 – Processing parameters
SI              32768
SF         500.1300000 MHz
WDW                EM
SSB                 0
LB              0.30 Hz
GB                  0
PC              1.00
```

COMPOUND A3



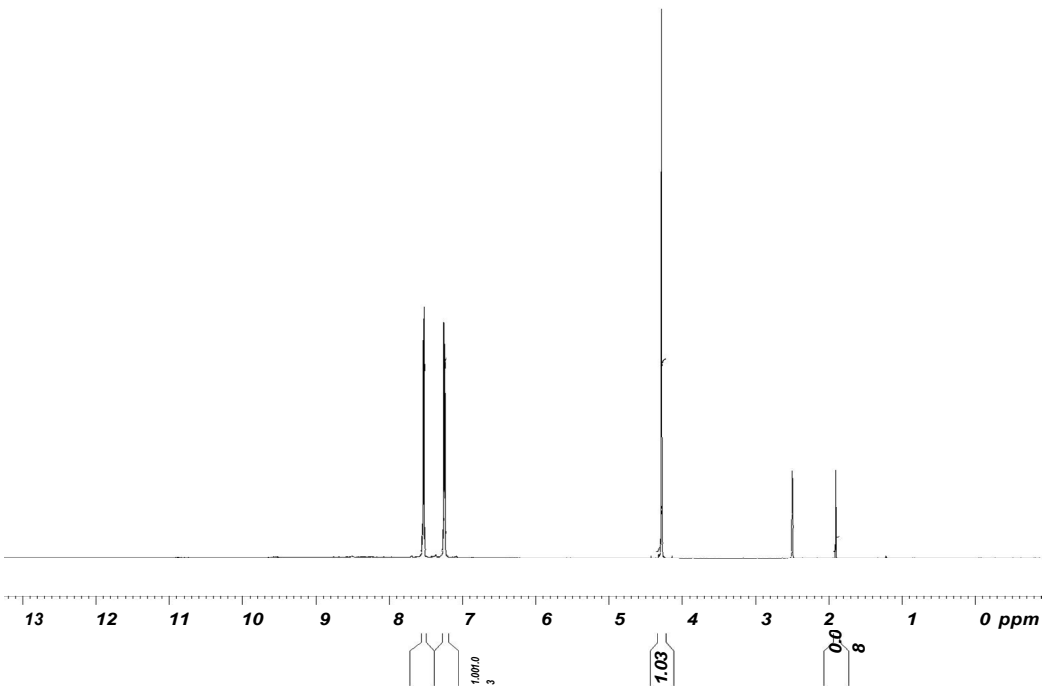

```
Current Data Parameters
NAME          Feb07-2014
EXPNO              21
PROCNO              1

F2 - Acquisition Parameters
Date_         20140207
Time              13.02
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG           zg30
TD               32768
SOLVENT           DMSO
NS                  32
DS                   2
SWH          10330.578 Hz
FIDRES        0.315264 Hz
AQ           1.5860212 sec
RG                 114
DW              48.400 usec
DE               6.50 usec
TE               300.2 K
D1           1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1               1H
P1              10.65 usec
PL1              0.00 dB
PL1W       23.53637505 W
SFO1       500.1330885 MHz

F2 - Processing parameters
SI               32768
SF         500.1300043 MHz
WDW                EM
SSB                 0
LB               0.30 Hz
GB                  0
PC                1.00
```

COMPOUND A4



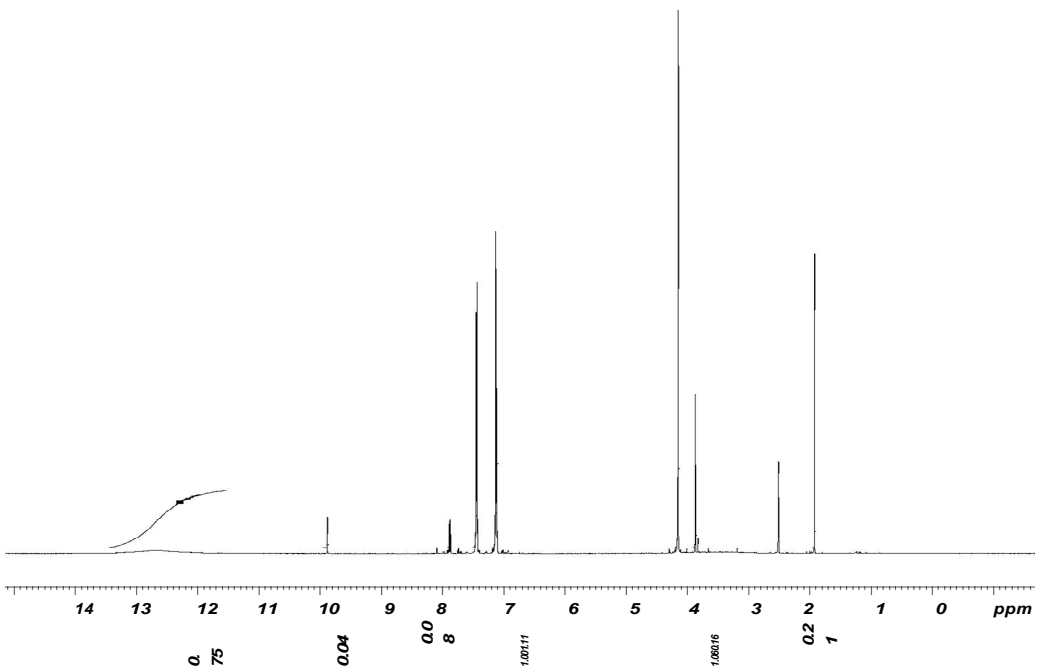

```
Current Data Parameters
NAME          Feb07-2014
EXPNO              27
PROCNO              1

F2 - Acquisition Parameters
Date_         20140207
Time              15.28
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG           zg30
TD               32768
SOLVENT           DMSO
NS                  32
DS                   2
SWH          10330.578 Hz
FIDRES        0.315264 Hz
AQ           1.5860212 sec
RG                 181
DW              48.400 usec
DE               6.50 usec
TE               300.5 K
D1           1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1               1H
P1              10.65 usec
PL1              0.00 dB
PL1W       23.53637505 W
SFO1       500.1330885 MHz

F2 - Processing parameters
SI               32768
SF         500.1300042 MHz
WDW                EM
SSB                 0
LB               0.30 Hz
GB                  0
PC                1.00
```

COMPOUND A5



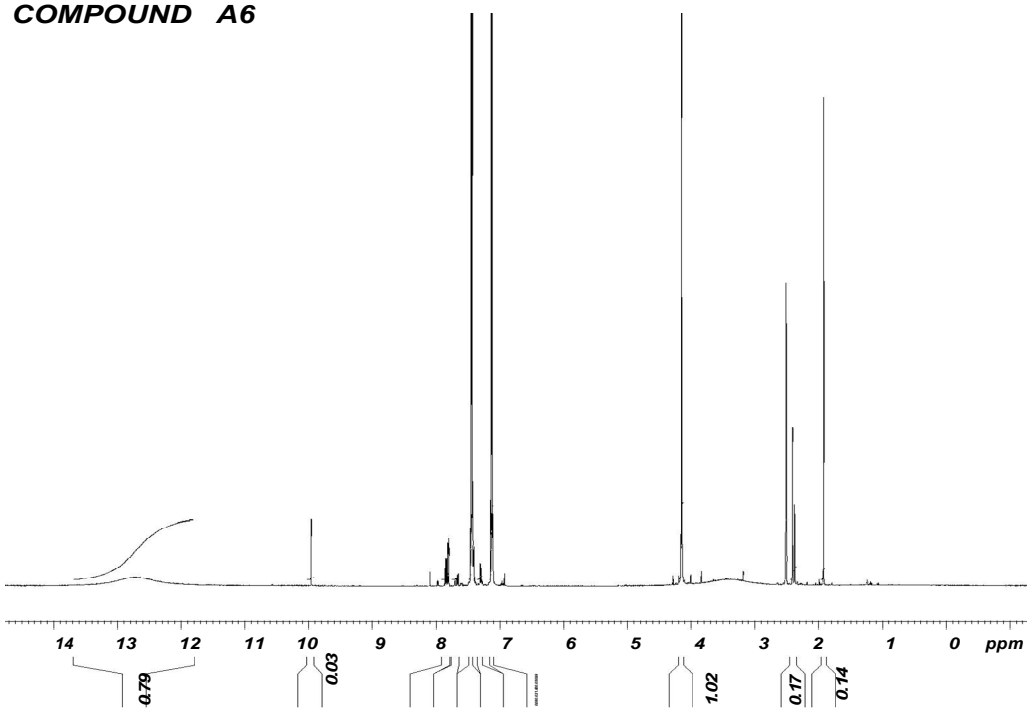
Current Data Parameters
NAME Feb07−2014
EXPNO 29
PROCNO 1

F2 − Acquisition Parameters
Date_ 20140207
Time 16.17
INSTRUM spect
PROBHD 5 mm PABBO BB−
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 32
DS 2
SWH 10330.578 Hz
FIDRES 0.315264 Hz
AQ 1.5860212 sec
RG 181
DW 48.400 usec
DE 6.50 usec
TE 300.6 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 10.65 usec
PL1 0.00 dB
PL1W 23.53637505 W
SFO1 500.1330885 MHz

F2 − Processing parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

COMPOUND A6



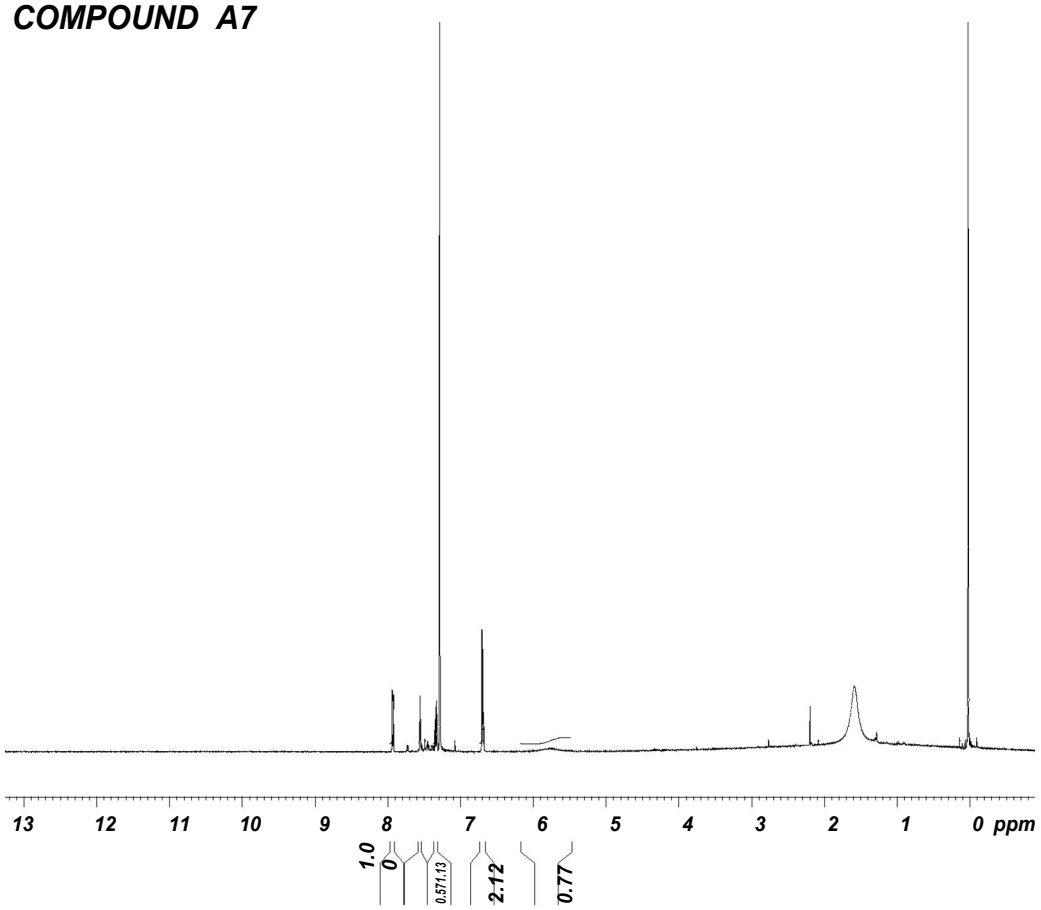
Current Data Parameters
NAME Feb07−2014
EXPNO 23
PROCNO 1

F2 − Acquisition Parameters
Date_ 20140207
Time 03.51
INSTRUM spect
PROBHD 5 mm PABBO BB−
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 32
DS 2
SWH 10330.578 Hz
FIDRES 0.315264 Hz
AQ 1.5860212 sec
RG 203
DW 48.400 usec
DE 6.50 usec
TE 300.3 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 10.65 usec
PL1 0.00 dB
PL1W 23.53637505 W
SFO1 500.1330885 MHz

F2 − Processing parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

COMPOUND A7



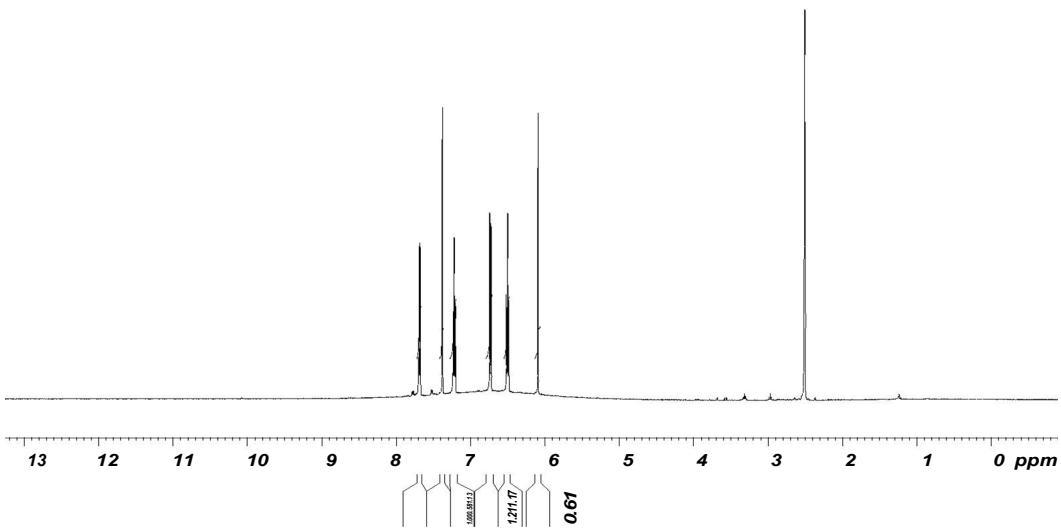
Current Data Parameters
NAME Feb08−2014
EXPNO 27
PROCNO 1

F2 − Acquisition Parameters
Date_ 20140208
Time 4.52
INSTRUM spect
PROBHD 5 mm PABBO BB−
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 32
DS 2
SWH 10330.578 Hz
FIDRES 0.315264 Hz
AQ 1.5860212 sec
RG 203
DW 48.400 usec
DE 6.50 usec
TE 299.3 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 10.65 usec
PL1 0.00 dB
PL1W 23.53637505 W
SFO1 500.1330885 MHz

F2 − Processing parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

COMPOUND A8



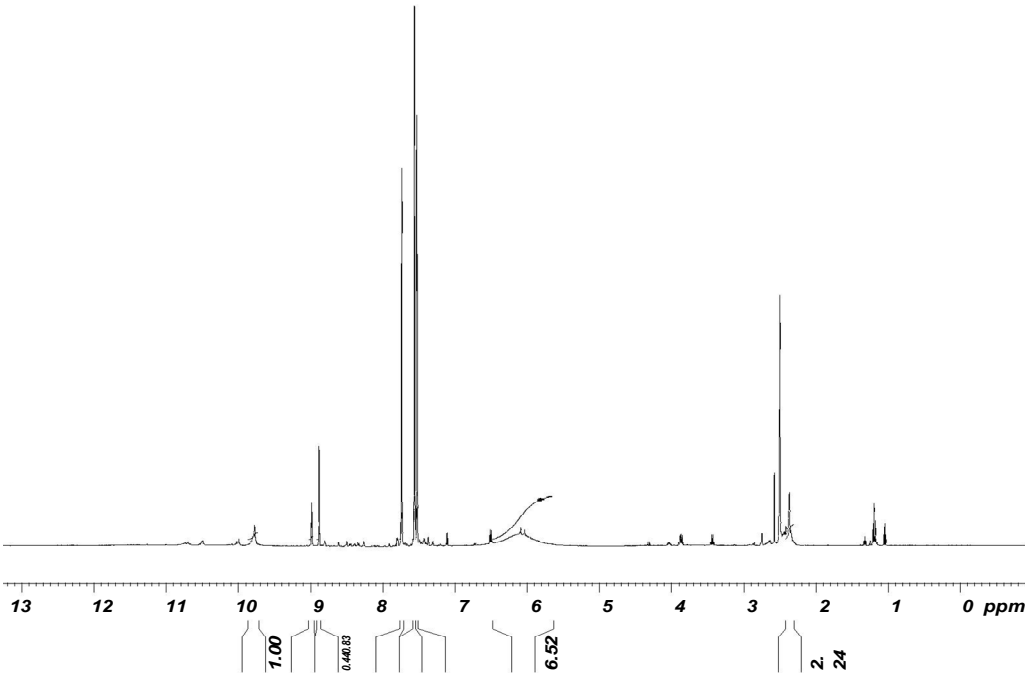
Current Data Parameters
NAME Feb08−2014
EXPNO 5
PROCNO 1

F2 − Acquisition Parameters
Date_ 20140208
Time 21.49
INSTRUM spect
PROBHD 5 mm PABBO BB−
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 32
DS 2
SWH 10330.578 Hz
FIDRES 0.315264 Hz
AQ 1.5860212 sec
RG 203
DW 48.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 10.65 usec
PL1 0.00 dB
PL1W 23.53637505 W
SFO1 500.1330885 MHz

F2 − Processing parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

COMPOUND A-9



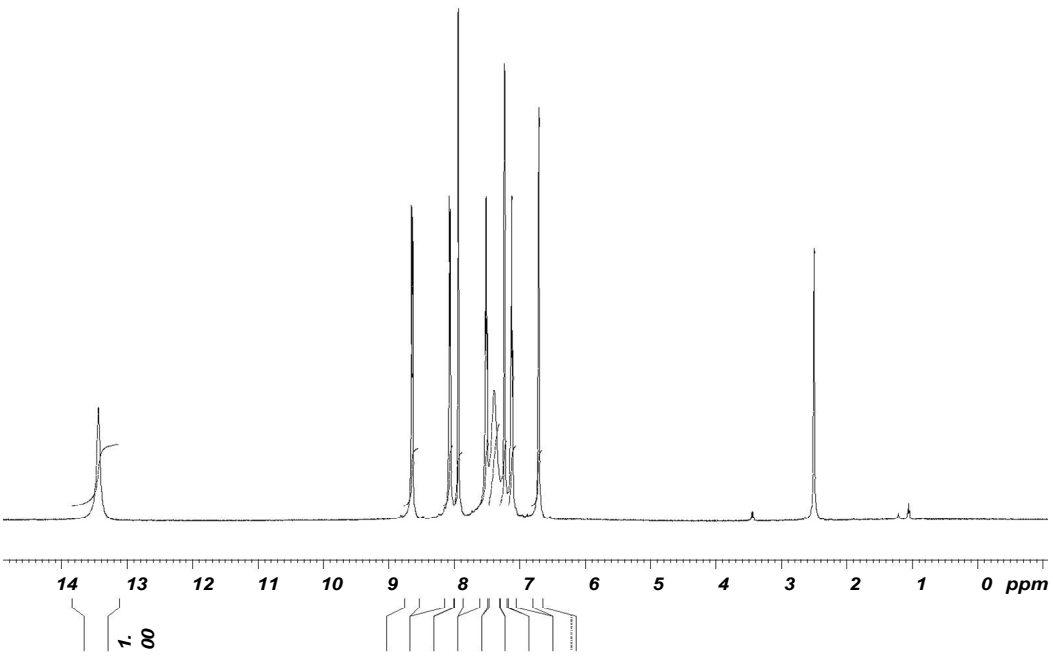

```
Current Data Parameters
NAME          Feb08-2014
EXPNO              23
PROCNO              1

F2 - Acquisition Parameters
Date_         20140208
Time            4.36
INSTRUM          spect
PROBHD    5 mm PABBO BB-
PULPROG          zg30
TD              32768
SOLVENT          DMSO
NS                 32
DS                  2
SWH         10330.578 Hz
FIDRES       0.315264 Hz
AQ          1.5860212 sec
RG                203
DW             48.400 usec
DE              6.50 usec
TE             299.3 K
D1          1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1               1H
P1              10.65 usec
PL1              0.00 dB
PL1W        23.53637505 W
SFO1        500.1330885 MHz

F2 - Processing parameters
SI              32768
SF         500.1300040 MHz
WDW                EM
SSB                 0
LB               0.30 Hz
GB                  0
PC               1.00
```

COMPOUND A10




```
Current Data Parameters
NAME          Feb08-2014
EXPNO              11
PROCNO              1

F2 - Acquisition Parameters
Date_         20140208
Time            22.10
INSTRUM          spect
PROBHD    5 mm PABBO BB-
PULPROG          zg30
TD              32768
SOLVENT          DMSO
NS                 32
DS                  2
SWH         10330.578 Hz
FIDRES       0.315264 Hz
AQ          1.5860212 sec
RG                203
DW             48.400 usec
DE              6.50 usec
TE             300.1 K
D1          1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1               1H
P1              10.65 usec
PL1              0.00 dB
PL1W        23.53637505 W
SFO1        500.1330885 MHz

F2 - Processing parameters
SI              32768
SF         500.1300035 MHz
WDW                EM
SSB                 0
LB               0.30 Hz
GB                  0
PC               1.00
```

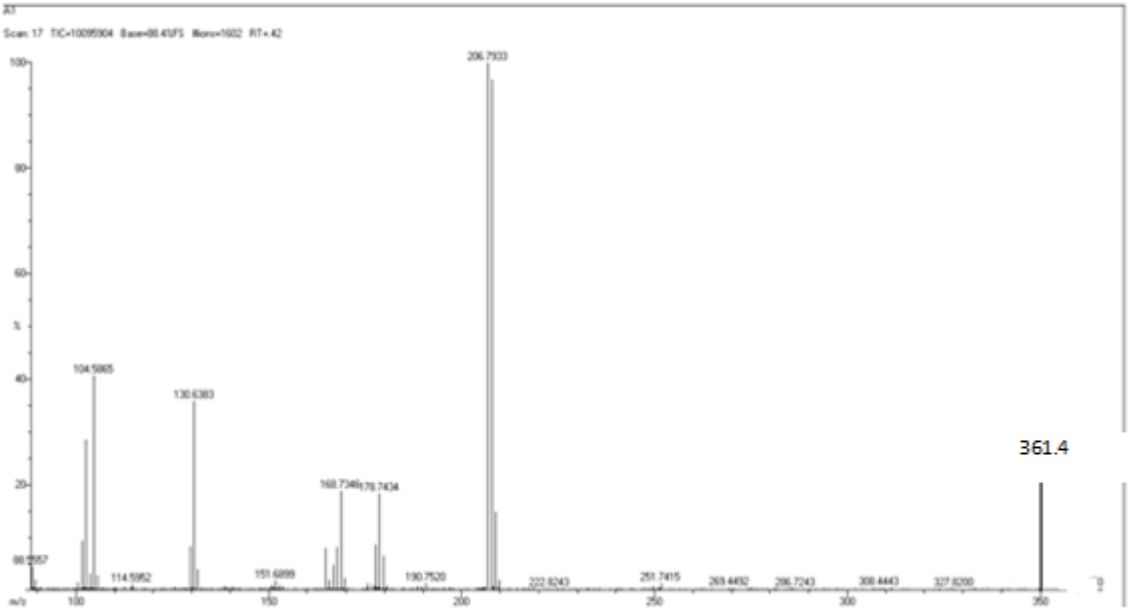
NMR DATAS

Table No. 7

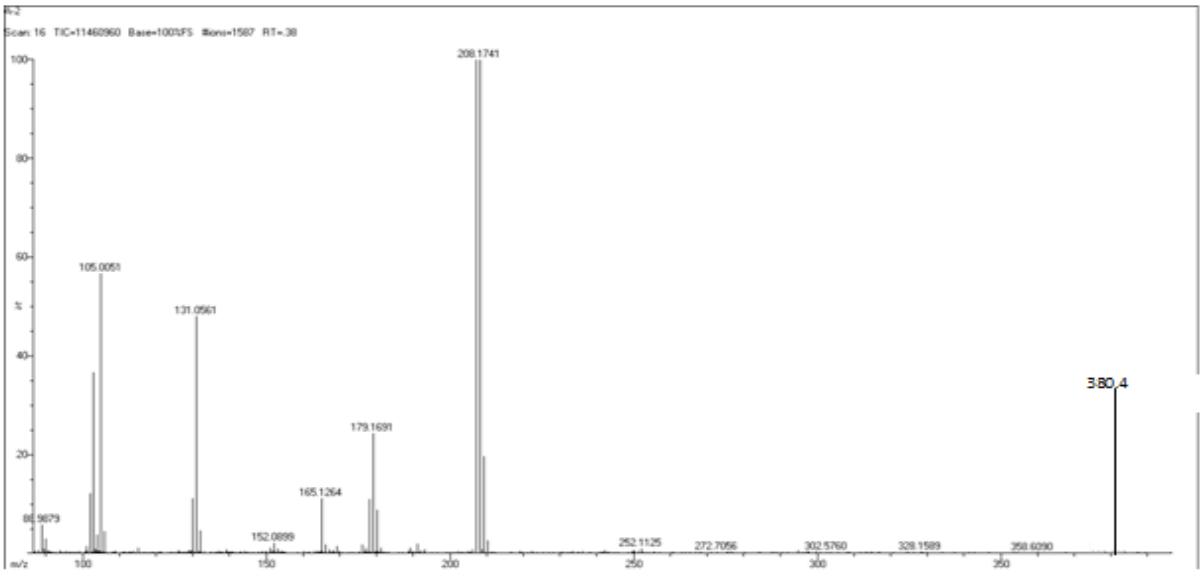
COMPOUND	TYPES OF PROTON	OBSERVEDVALUE in PPM
A1	S,15H ArH M,2H CH	8.8 7.7
A2	S,15H ArH S, 1H,NH	8.1 2.1
A3	S, 15H ArH S, 10H ArH	7.1 7.7
A4	S,15H ArH S,2H CH	7.0 7.5
A5	S, 10H ArH S,N-CH3	7.6 4.3
A6	S,15H ArH M,2H CH	7.4 8.0
A7	S,15H CH S, 1H ,NH	7.1 2.1
A8	S, 15H ArH S,10H ArH	7.3 7.9
A9	S,15H ArH S, 2H CH	7.8 9.1
A10	S,15H ArH S,N-CH3	8.9 6.9

MASS SPECTROSCOPY

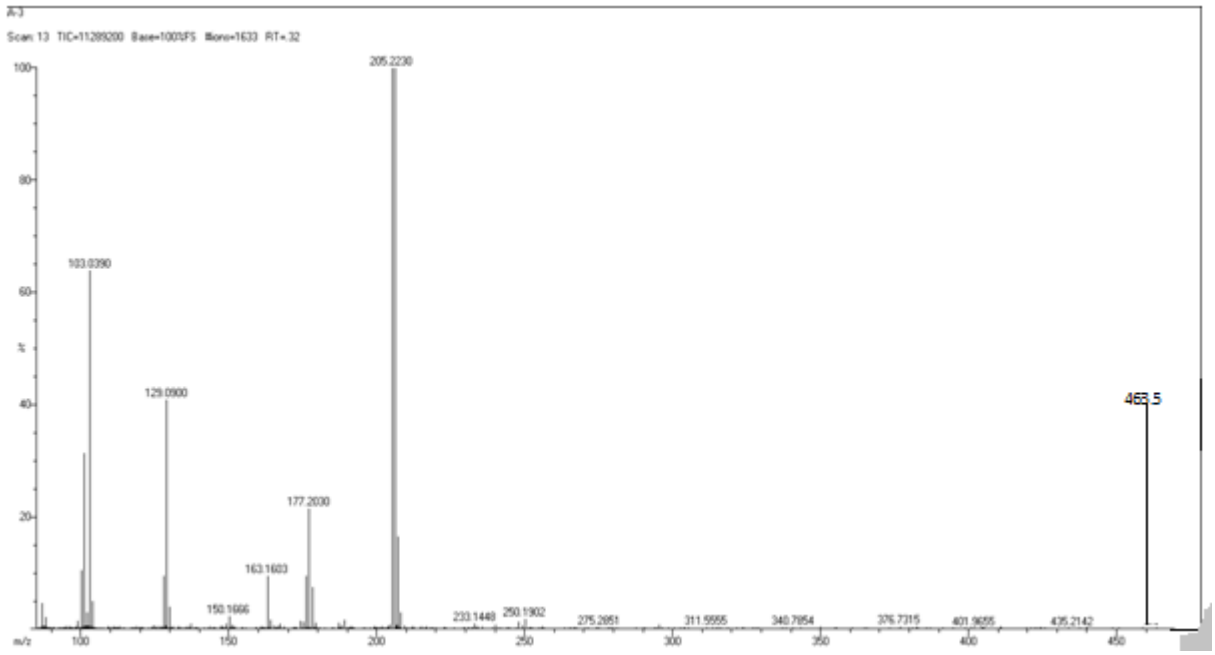
COMPOUND A1



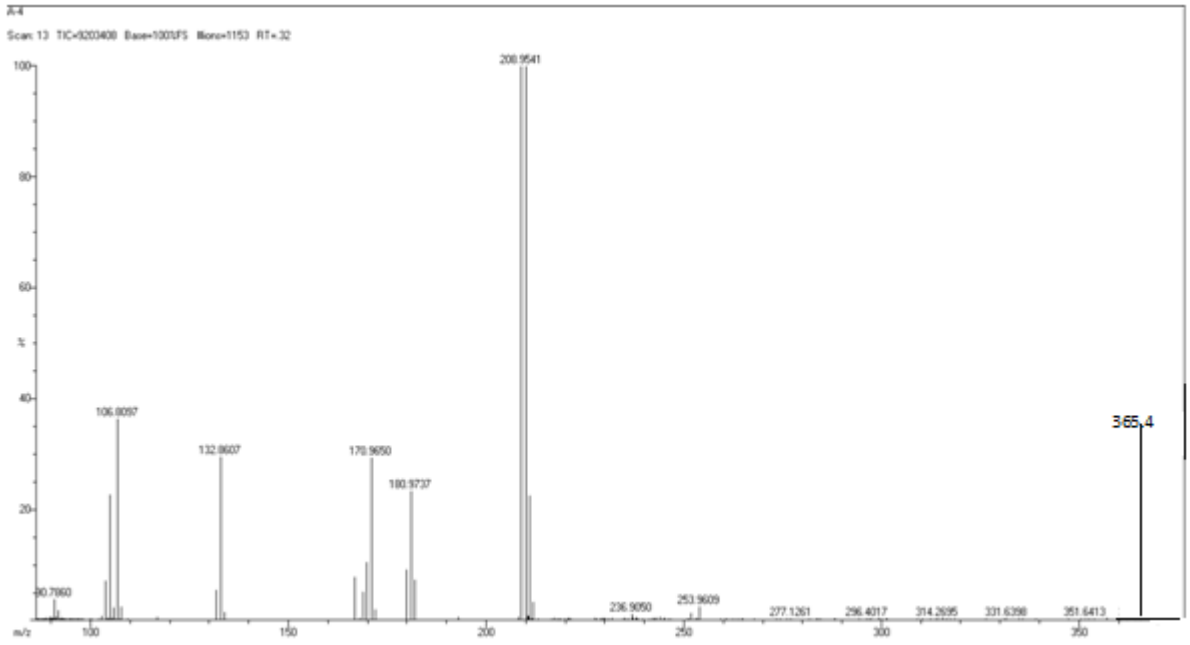
COMPOUND A2



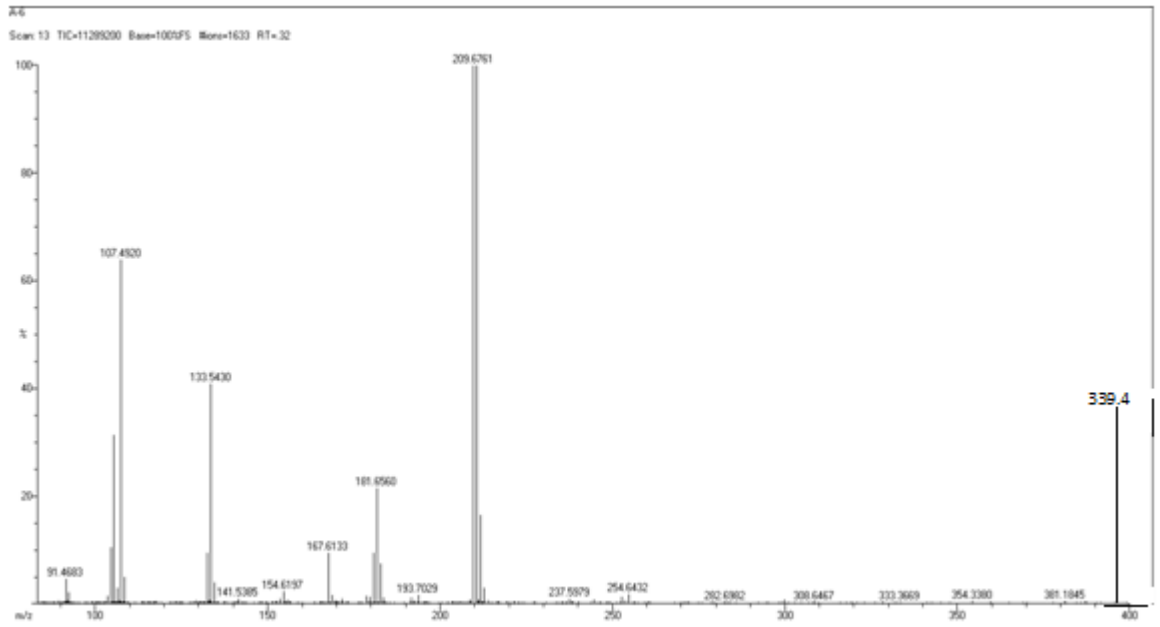
COMPOUND A3



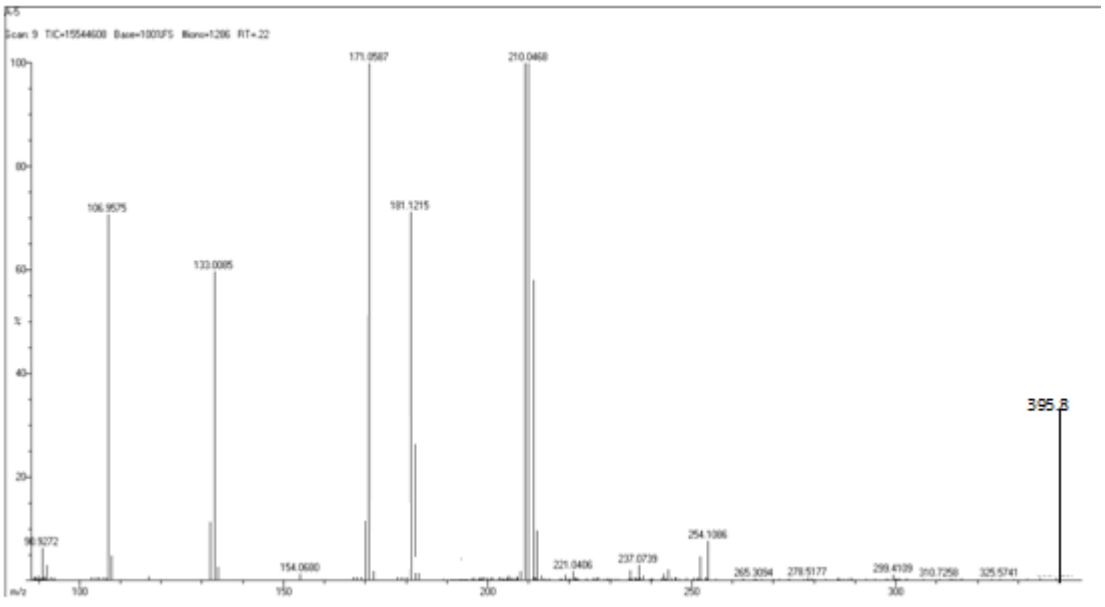
COMPOUND A4



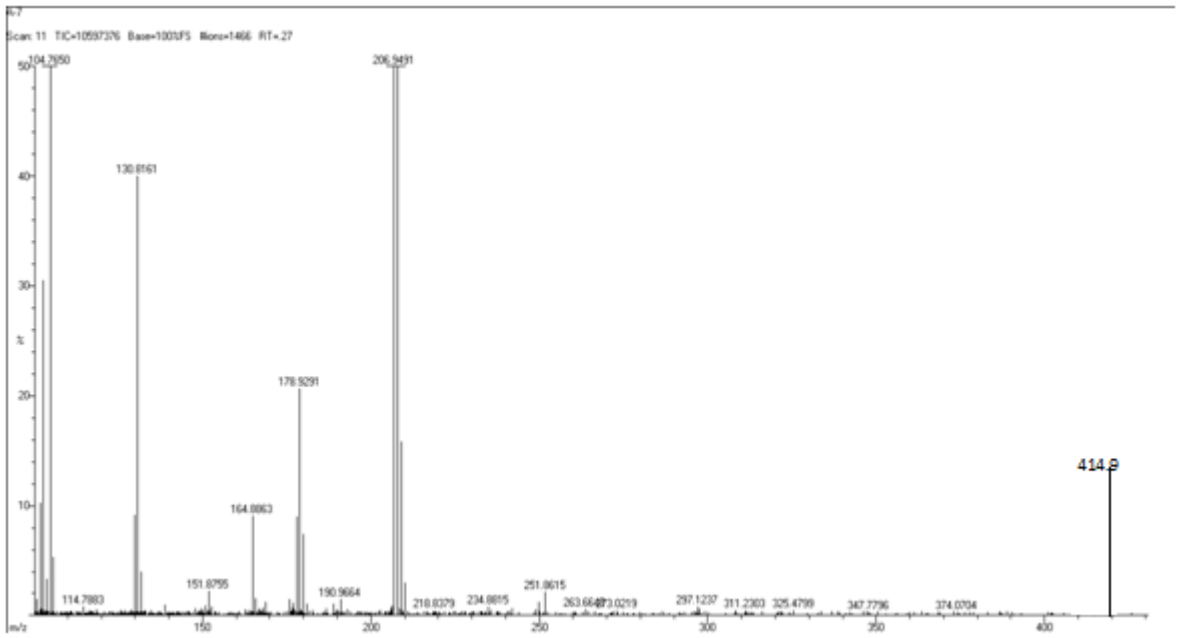
COMPOUND A5



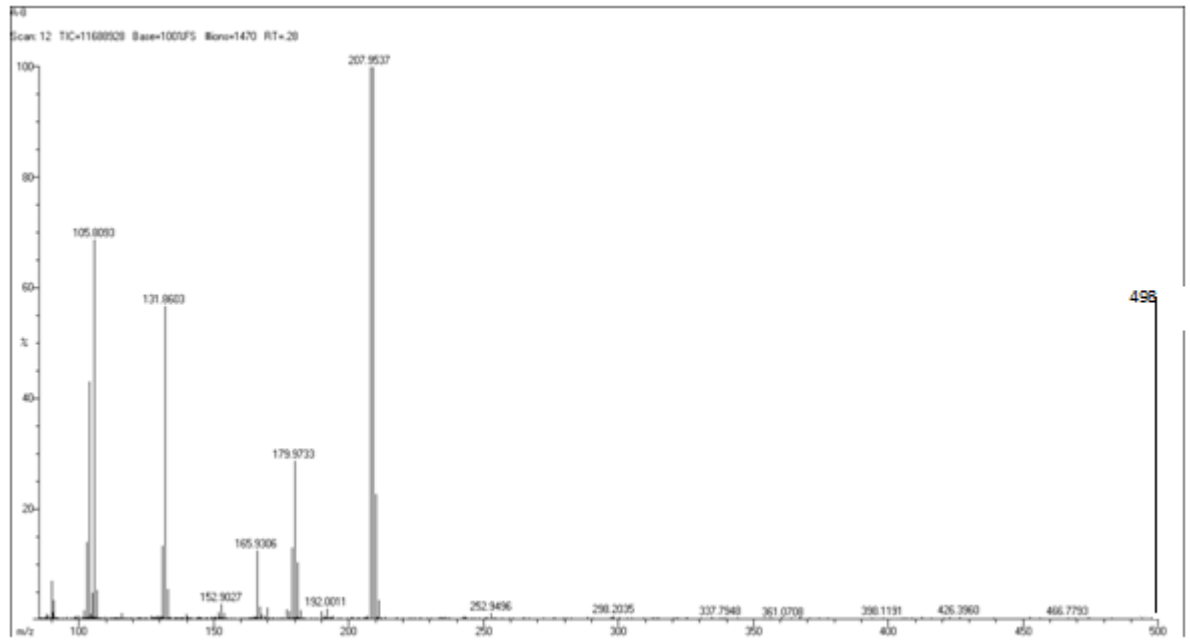
COMPOUND A6



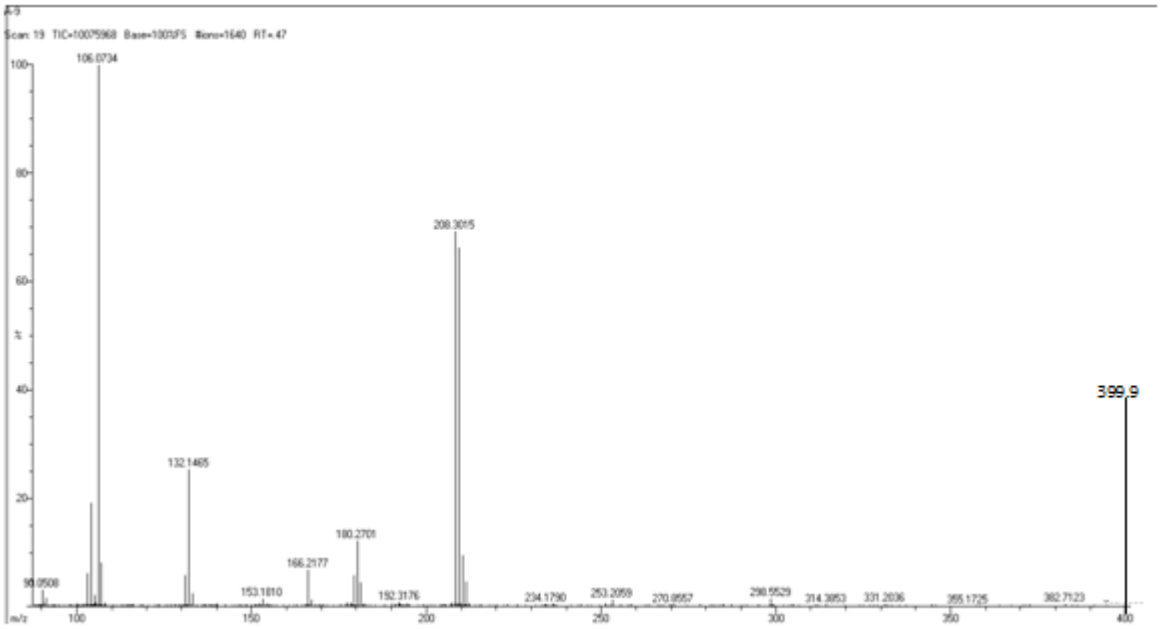
COMPOUND A7



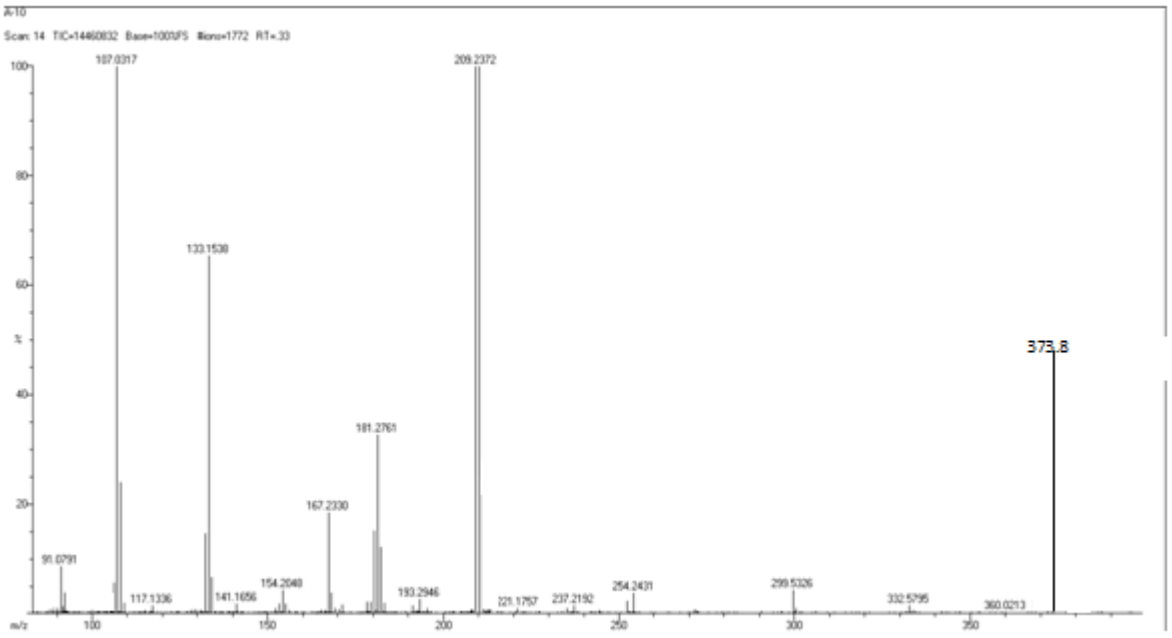
COMPOUND A8



COMPOUND A9



COMPOUND A10



MASS SPECTRAL DATAS

Table.No:8

COMPOUND	OBSERVED PEAK
A1	361.4
A2	380.4
A3	463.5
A4	365.4
A5	339.4
A6	395.8
A7	414.9
A8	498
A9	399.9
A10	373.8

BIOLOGICAL EVALUATION

BIOLOGICAL EVALUATION

IN VITRO- ANTIBACTERIAL ACTIVITY[21,25,42,51-53]

TEST CONCENTRATION:

- 100µg/ml
- 200µg/ml

ORGANISM USED:

- Bacillus subtilis
- Klebsiella pneumonia

SOLVENT USED:

- DMSO

STANDARD DRUG:

- Amikacin

MEDIA PREPARATION:

MULLER- HINTON AGAR MEDIUM:

INGREDIENTS:

Beef infusion	- 300ml
Casein Hydrolysate	- 17.5g
Starch	- 1.5g
Agar	- 10g
Distilled water	- 1litr

PROCEDURE:

Emulsify the starch in a small amount of cold water, pour into the beef infusion and add the casein hydrolysate and the agar. Make up the volume to 1litre with distilled water. Dissolve the constituents by heating gently at 100°C with agitation. Filter if necessary. Adjust the pH to 7.4.Dispense in screw-capped bottles and sterilized by autoclaving at 121°C for 20minutes and pour plates.

PREPARATION OF ANTIBACTERIAL SOLUTION:

All the test compound were dissolved in dimethyl sulfoxide and taken at two concentration for testing antibacterial activity. The compounds were diffuse into the medium produced a concentration gradient. After the incubation period, the zone of inhibition were measured in mm.

EXPERIMENTAL PROCEDURE:

The plates were inoculated by dipping a sterile swab into inoculums. The inoculation was dried at room temperature in aseptic condition. Ditch the bore in plate, to this bore add prepared antibacterial solution. These plates were placed in an incubator at 37°C within a few minutes of preparation. After 48 hours of incubation the diameter of zone of inhibition was measured and reading observed in millimeter.

ZONE OF INHIBITION OF SYNTHESIZED COMPOUNDS AGAINST BACTERIA

Table.No:9

SAMPLE	BACILLUS		KLEBSIELLA	
	100µg/ml	200µg/ml	100µg/ml	200µg/ml
A1	R	9	R	R
A2	6	17	R	12
A3	10	15	R	10
A4	8	14	R	8
A5	11	16	R	12
A6	R	9	R	R
A7	15	21	8	17
A8	R	12	R	9
A9	R	14	R	R
A10	7	16	R	6
CONTROL	R	R	R	R
STD	17	17	20	20

ALL MEASUREMENT IN{ MMS }

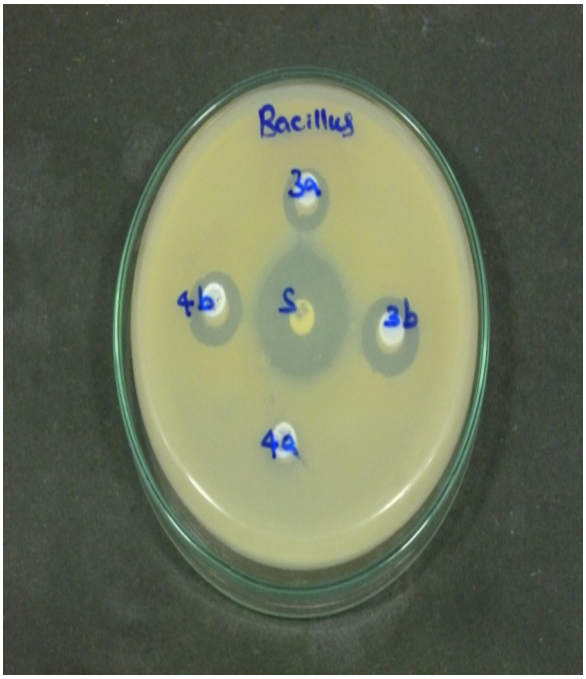
R = RESISTANT

CONTROL= DMSO

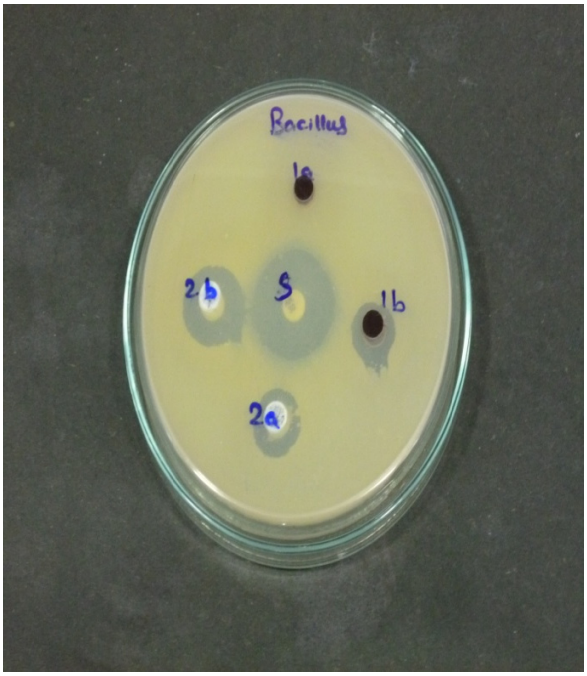
STD = AMIKACIN

ANTIBACTERIAL ACTIVITY

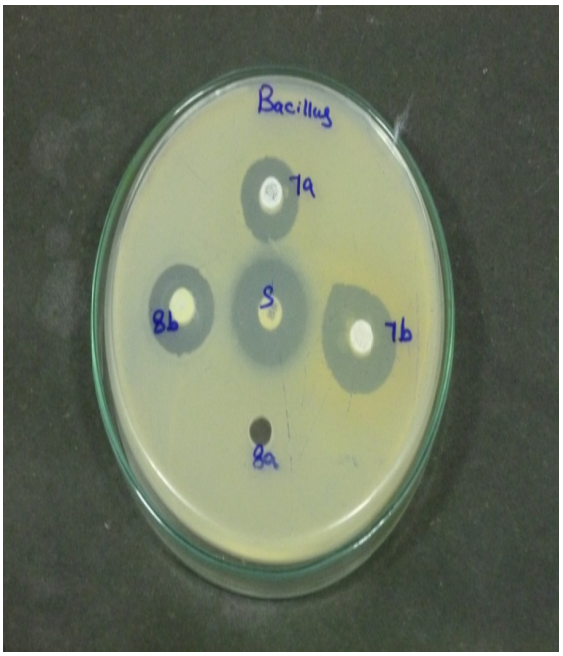
BACILLUS SUBTILIS –A3, A4



BACILLUS SUBTILIS –A1, A2



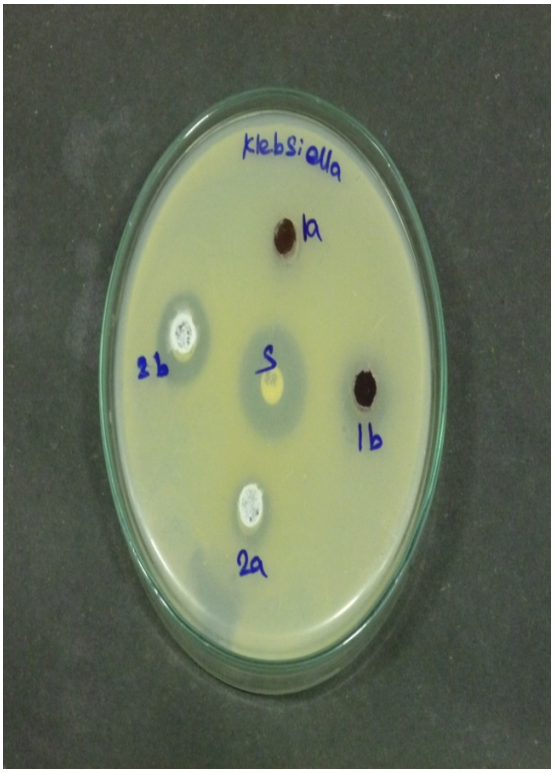
BACILLUS SUBTILIS – A7, A8

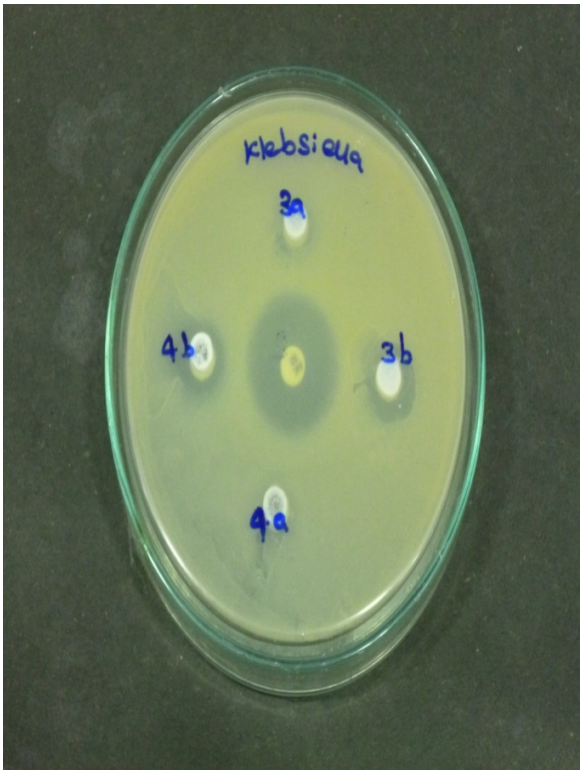


BASCILLUS SUBTILIS - CONTROL

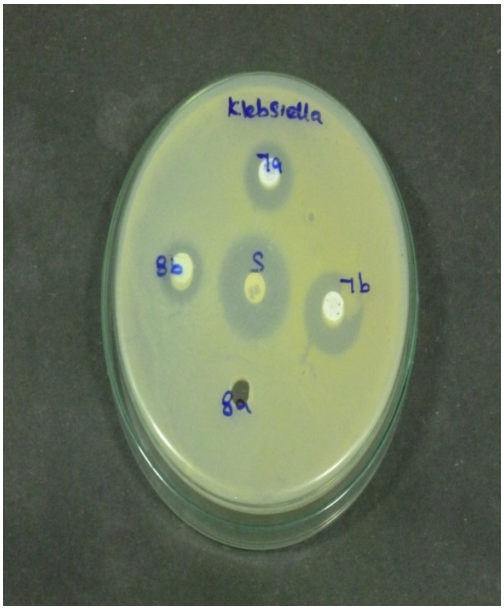
ANTIBACTERIAL ACTIVIT

KLEBSIELLA PNEUMONIA –A1, A2 KLEBSIELLA PNEUMONIA–A3, A4

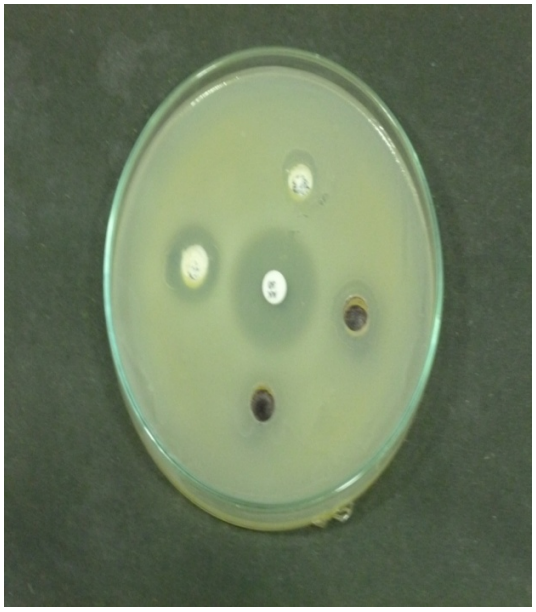




KLEBSIELLA PNEUMONIA –A7,A8



KLEBSIELLA – CONTROL



ANTIFUNGAL ACTIVITY[21,25,42,51-53]

TEST CONCENTRATION:

- 100µg/ml
- 200µg/ml

ORGANISM USED:

- Candida Albicans
- Aspergillus Niger

SOLVENT USED:

- DMSO

STANDARD DRUG:

- Ketokonazole

MEDIA PREPARATION:

POTATO DEXTROSE AGAR MEDIUM

INGREDIENTS:

Potato	- 200g
Dextrose	- 20g
Agar	- 20g
Water	- 1litre

PROCEDURE:

Scrub but do not peel the potatoes and cut into 12mm cubes. Boil 200g potato in 1litre of water for 60 minutes. Squeeze as much of the pulp as possible through a fine sieve. Add agar and boil till dissolved. Add dextrose and make up to 1litre. Dispense in required amounts taking care to keep solids in suspension. Autoclave at 115°C and pour approximately 20ml amounts into petri dishes.

PREPARATION OF ANTI FUNGAL SOLUTION:

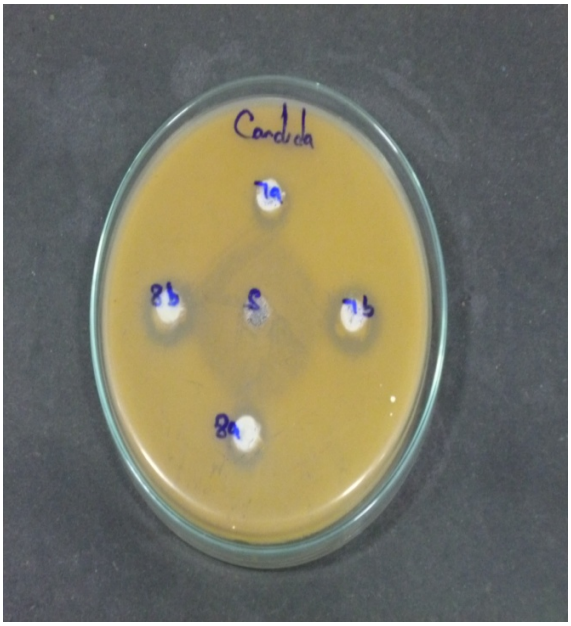
All the test compound were dissolved in dimethyl sulfoxide and taken at two concentration for testing antibacterial activity. The compounds were diffuse into the medium produced a concentration gradient. After the incubation period, the zone of inhibition were measured in mm.

EXPERIMENTAL PROCEDURE:

The plates were inoculated by dipping a sterile swab into inoculums. The inoculation was dried at room temperature in aseptic condition. Ditch the bore in plate, to this bore add prepared antibacterial solution. These plates were placed in an incubator at 22°C within a few minutes of preparation. After 7 days of incubation the diameter of zone of inhibition was measured and reading observed in millimeter.

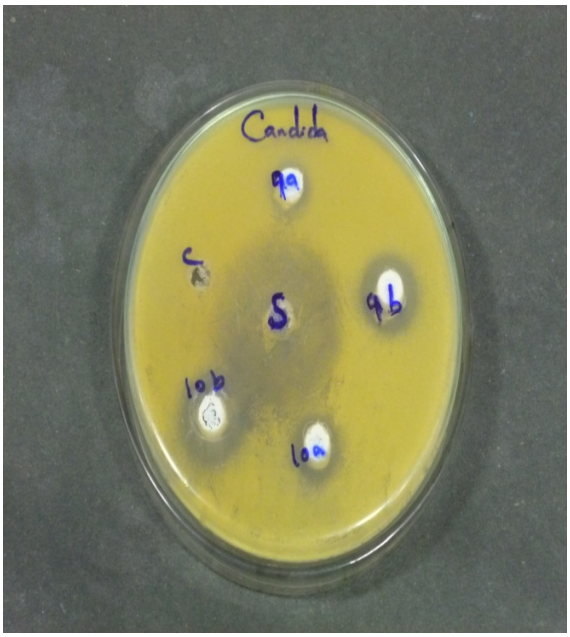
ANTIFUNGAL ACTIVITY

CANDIDA ALBICANS – A7, A8



CANDIDA ALBICANS – A1, A2

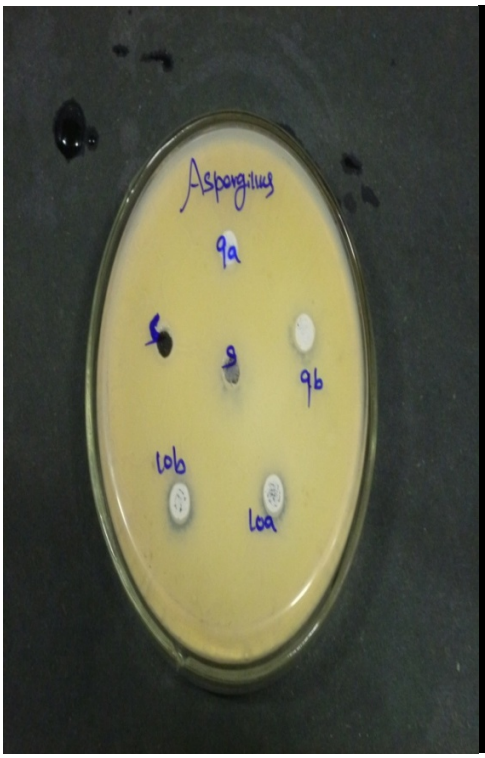
CANDIDA ALBICANS – A9,A10



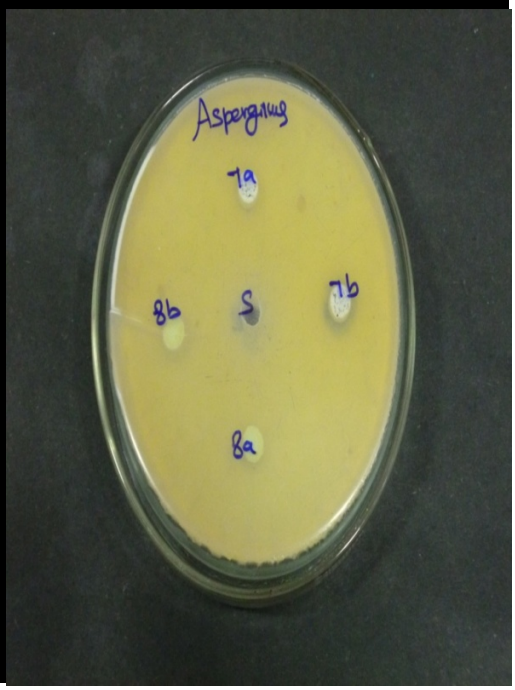
CANDIDA ALBICANS – CONTROL

ANTIFUNGAL ACTIVITY

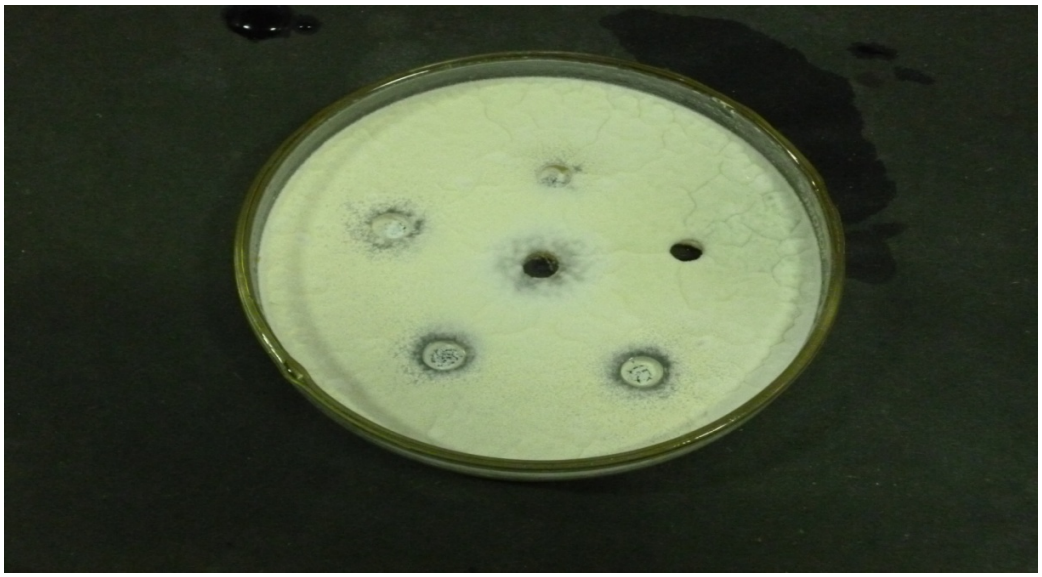
ASPERGILLUS NIGER A9, A10



ASPERGILLUS NIGER A7, A8



ASPERGILLUS NIGER - CONTROL



ZONE OFINHIBITION OF SYNTHESIZED COMPOUNDS AGAINST FUNGI

Table.No:10

SAMPLE	CANDIDA		ASPERGILLUS	
	100µg/ml	200µg/ml	100µg/ml	200µg/ml
A1	3	7	R	R
A2	R	6	R	R
A3	R	10	R	R
A4	R	8	R	R
A5	5	11	R	R
A6	R	9	R	R
A7	R	7	R	9
A8	5	9	R	R
A9	5	12	R	6
A10	5	12	R	8
CONTROL	R	R	R	R
STD	21	21	18	18

ALL MEASUREMENT IN{ MMS }

R = RESISTANT

CONTROL = DMSO

STD = KETOKONAZOLE

ZONE OF MAXIMUM INHIBITION OFSYNTHESIZED

COMPOUND A1- A10 AGAINST MICROBIAL AGENTS

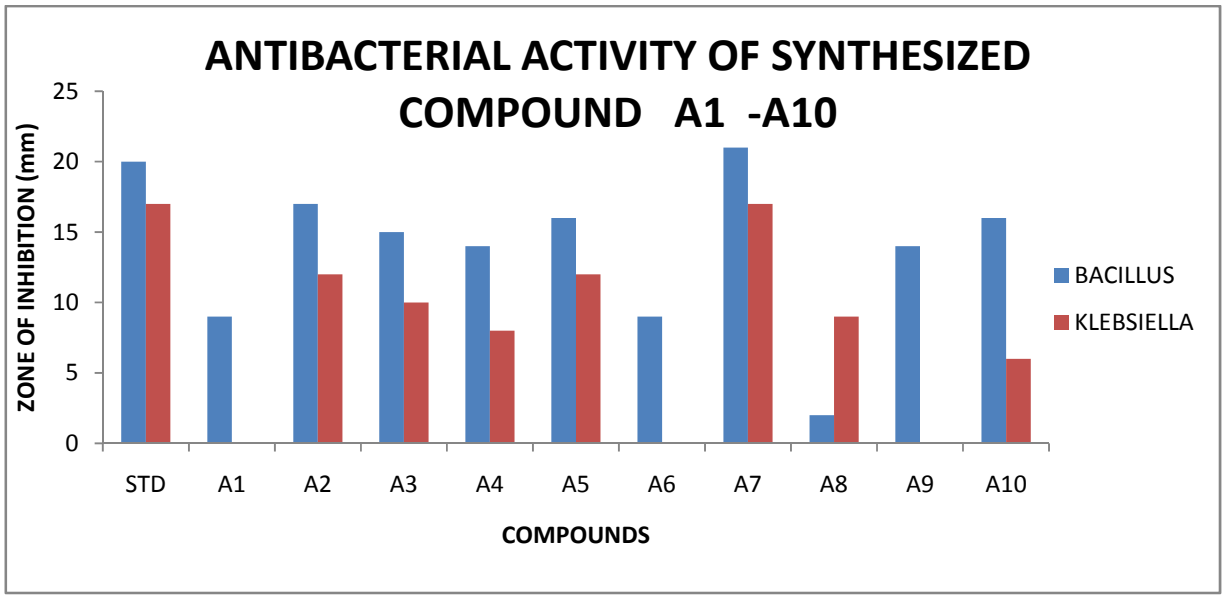
Table.No:11

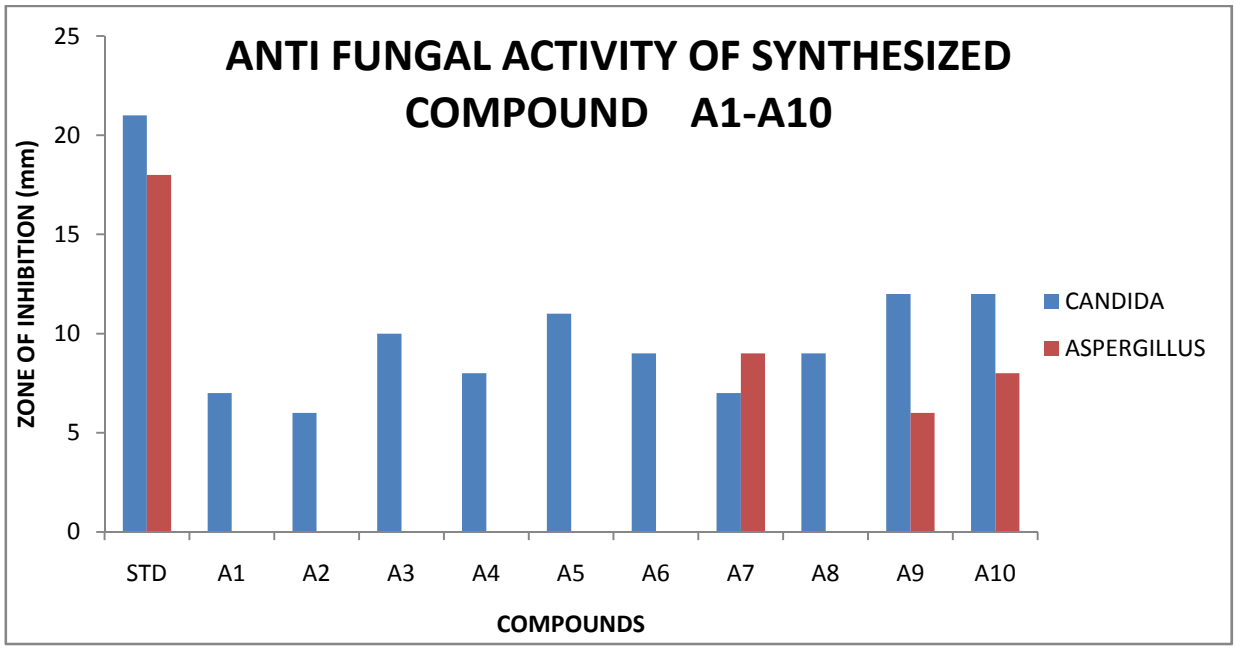
ORGANISM	BACTERIA		FUNGI	
COMPOUNDS	BACILLUS	KLEBSIELLA	CANDIDA	ASPERGILLUS
A1	9	-	7	-
A2	17	12	6	-
A3	15	10	10	-
A4	14	8	8	-
A5	16	12	11	-
A6	9	-	9	-
A7	21	17	7	9
A8	12	9	9	-
A9	14	-	12	6
A10	16	6	12	8
STD	20	17	21	18

Zone of inhibition in mm

STD: BACTERIA – AMIKACIN, FUNGI - KETAKONAZOLE

INVITRO - ANTI MICROBIAL ACTIVITY



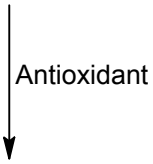


IN VITRO-ANTIOXIDANT ACTIVITY[54,56,57]

PRINCIPLE:

This is spectrophotometric method and is based on the principle that increases in absorbance of the reaction mixture as concentration increase showing an increased antioxidant activity. The assay is based on the reduction of ferric in potassium ferric cyanide to potassium ferrocyanide by the sample and the subsequent formation of Prussian blue colour with ferric chloride. The absorbance of the blue complex is measured at 700nm.

Potassium ferric cyanide +Ferric chloride



Potassium ferrocyanide + ferrous chloride

INSTRUMENTS:

Shimadzu UV Visible spectroscopy

Model 1800

REAGENTS:

1%Potassium ferric cyanide

10% Trichloro acetic acid

0.2M, pH 6.6 phosphate buffer

0.1% ferric chloride

PROCEDURE:

- About 0.5ml of various concentration of synthesized compound was mixed with 0.75ml phosphate buffer and 0.75ml of 1% potassium ferricyanide then mixture was incubated at 50°C for 20 minutes.
- 0.75ml of 1% trichloro acetic acid was added to the mixture, allowed to stand for 10 minutes.
- The whole mixture was then centrifuged at 3000ppm for 10 minutes.
- Finally 1.5ml of supernatant solution was removed and mixed with 1.5ml of distilled water
- Then added 0.1ml of 0.1%ferric chloride solution and the absorbance was measured at 700nm in UV – Visible spectrophotometry.
- Higher the absorbance observed in test mixture indicates the stronger reducing power of the test solution.
- Ascorbic acid was used as standard and phosphate buffer used as blank solution.
- The absorbance of the final reaction mixture of three parallel experiments was expressed as mean ± standard error of the mean.

IN VITRO -REDUCING POWER ASSAY

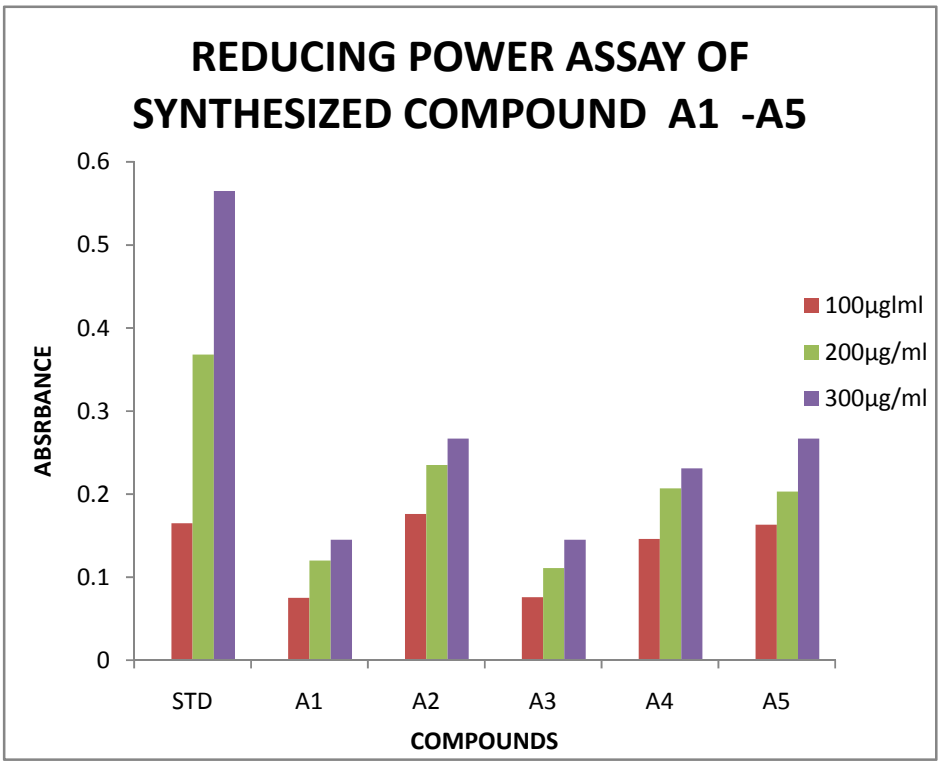
Table.No:12

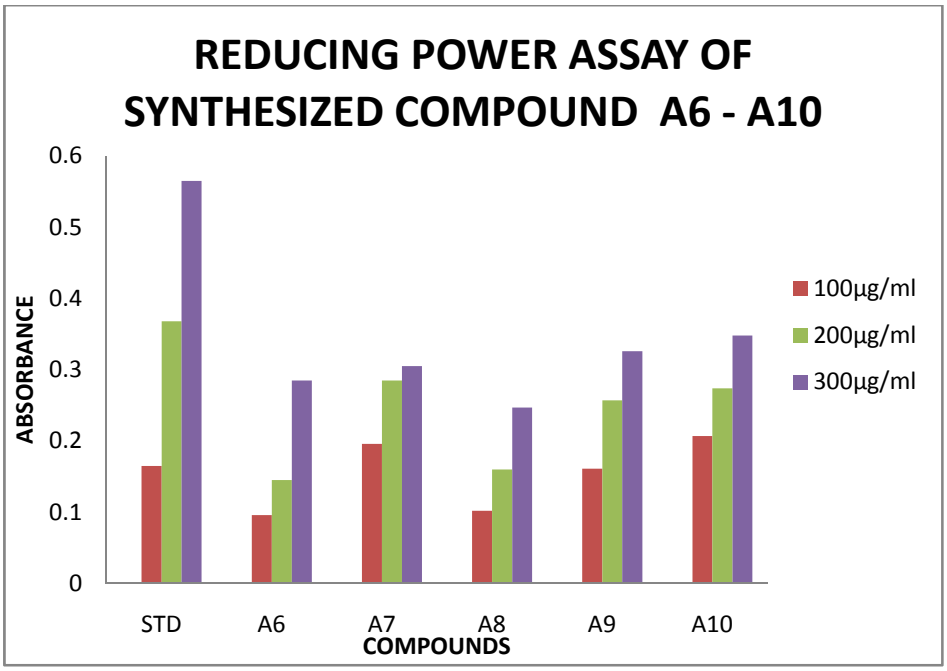
COMPOUNDS/ CONCENTRATION	ABSORBANCE*		
	100µg/ml	200µg/ml	300µg/ml
A1	0.075±0.0032	0.12±0.0011	0.145±0.0011
A2	0.172±0.0030	0.238±0.0037	0.269±0.0055
A3	0.076±0.0020	0.111±0.0011	0.140±0.0026
A4	0.146±0.0011	0.207±0.002	0.231±0.0017
A5	0.163±0.0038	0.203±0.002	0.267±0.0024
A6	0.096±o.0008	0.145±0.002	0.285±0.003
A7	0.196±0.0017	0.285±0.0023	0.305±0.005
A8	0.102±0.0014	0.160±0.002	0.247±0.0011
A9	0.161±0.0024	0.257±0.0024	0.326±0.0017
A10	0.207±0.00024	0.274±0.0011	0.348±0.0015
STD	0.165±0.0014	0.368±0.0025	0.565±0.0026

STD: ASCORBIC ACID

*Mean 3value±SEM

IN VITRO - ANTIOXIDANT ACTIVITY





IN VITRO - ANTI ARTHRITIC ACTIVITY[27,38,40,56]

Phosphate buffer saline pH 6.3:

Dissolve 8gm of sodium chloride 0.2gm of potassium chloride 1.44gm of disodium hydrogen phosphate 0.24 gm in potassium dihydrogen phosphate in 800 ml of distilled water. The pH was adjusted to 6.3 using 1N HCl make up the volume to 1000ml with distilled water.

METHOD:

1) Test solution (0.5ml) consists of 0.45ml of bovine serum (5% w/v aqueous solution)and 0.05ml of test solution various concentration.
2) Test control solution0.5ml consists of 0.45ml of bovine serum albumin and 0.05ml of water.
3) Product control 0.5ml consists of 0.45ml of water and 0.05ml of test solution.
4) Standard solution 0.5ml consists of 0.45ml of bovine serum albumin and 0.05ml of diclofenac sodium of various concentrations.
5) Various concentration (100,250,500µg/ml) of test drug and standard drug diclofenac sodium (100,250,500µg/ml)were taken respectively.
6) All the above solution were adjusted to pH 6.3 using 1N HCl.
7) The sample were incubated at 37°C for 20 minutes. Temperature was increased to keep the samples at 57°C for 3 minutes.
8) After cooling, add 2.5ml of phosphate buffer to the above solution.
9) The absorbance was measured using UV visible spectrophotometer at 416nm.

$$\text{Percentage inhibition} = 100 - \frac{\{\text{optical density of test control} - \text{optical Density of product control}\}}{\text{Optical density of test solution}} \times 100$$

IN VITRO – ANTIARTHRITIC ACTIVITY

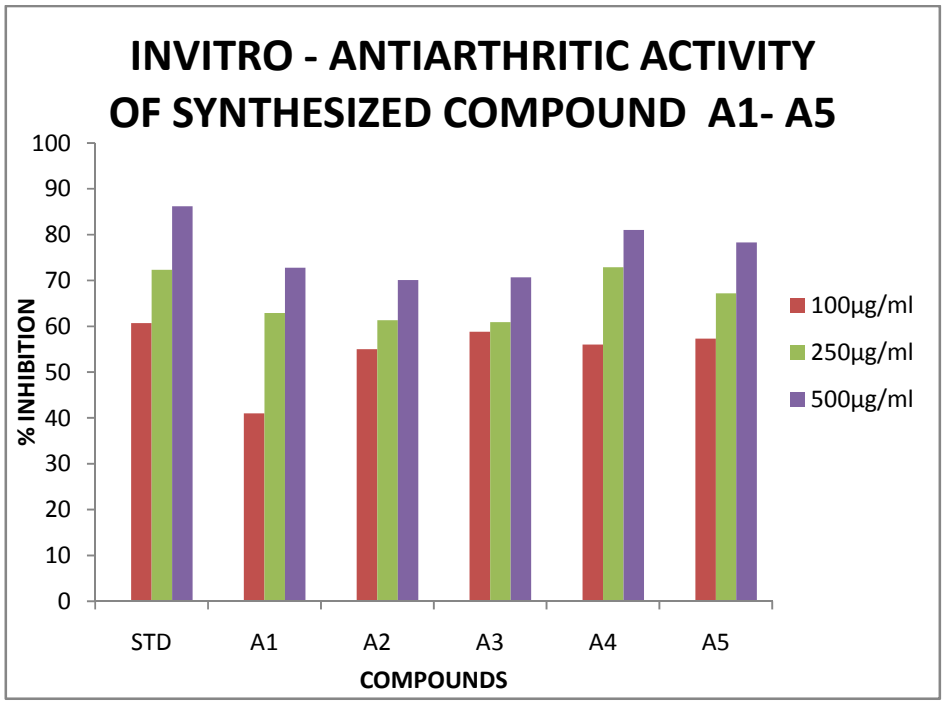
Table.No:13

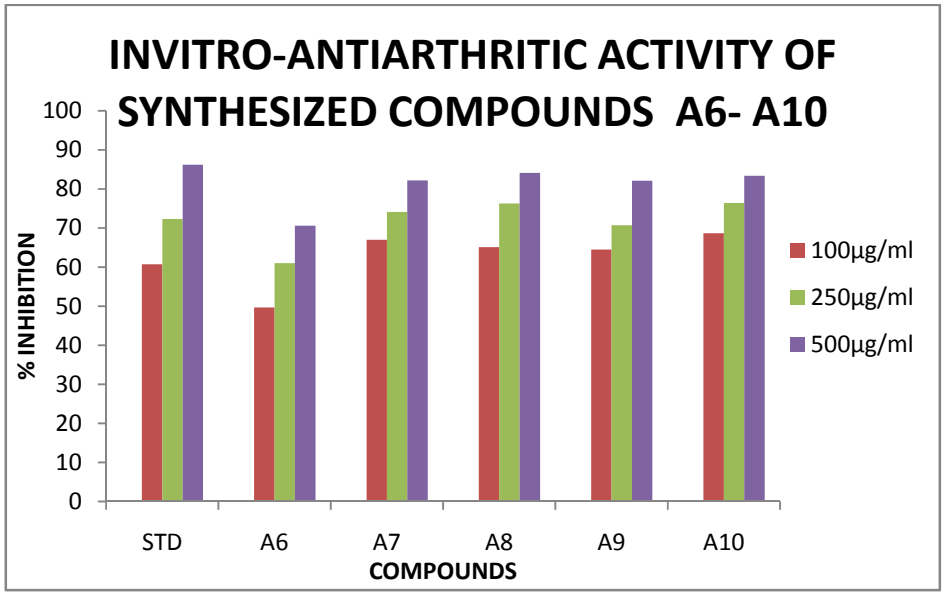
COMPOUNDS/ CONCENTRATION	% INHIBITION*		
	100µg/ml	**250µg/ml**	**500µg/ml**
A1	41±0.54	62.9±0.52	72.8±0.46
A2	55±0.0.46	61.3±0.53	70.1±0.40
A3	58.8±0.61	60.9±0.52	70.7±0.25
A4	56.5±0.28	72.9±0.31	81±0.23
A5	57.3±0.35	67.2±0.43	78.3±0.35
A6	49.7±0.21	61±0.460	70.6±0.31
A7	67±0.401	74.1±0.25	82.2±0.33
A8	65.1±0.20	76.3±0.35	84.1±0.21
A9	64.5±0.26	70.7±0.25	82.1±0.20
A10	68.7±0.20	76.4±0.26	83.4±0.32
STD	60.7±0.53	72.3±0.40	86.2±0.43

STD: DICLOFENAC

*Mean 3value ±SEM

IN VITRO - ANTI ARTHRITIC ACTIVITY





IN VIVO - ANTIANGIOGENIC ACTVITY

CHICKEN CHORIOALLANTOIC MEMBRANE (CAM) NEOVASCULARISATION MODEL IN THE FERTILIZED CHICKEN EGGS.

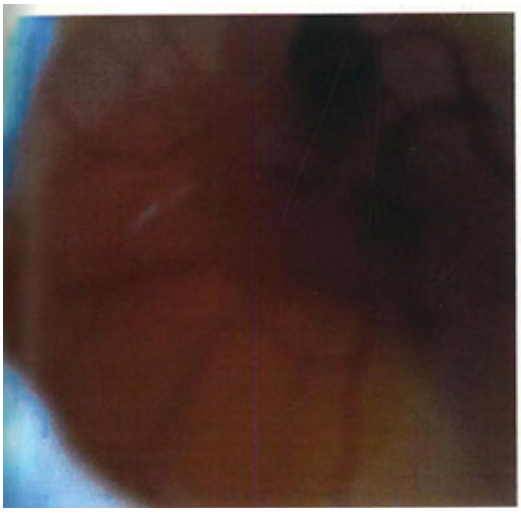
- The in vivo anti-angiogenic effect of the test compound was investigated by CAM assay.
- Fertilized chicken eggs of 5 days old were obtained from a local hatchery.
- Albumin 5 ml was with drawn and the eggs were incubated horizontally to allow the CAM detachment of the shell.
- The compound were dissolved in ethanol and prepared as methyl cellulose discs at the concentration of 50, 100µg/disc. Disc containing the vehicle alone (ethanol) were used as negative control.
- A small window was made on the shell through which the disc were applied the CAM.
- The window was closed back and sealed with a sterile surgical tap and the eggs were incubated for another 24 hrs.
- The images of each treated CAM were captured under dissecting microscope.
- The blood vessels in the disc application site were counted to calculate the percentage inhibition.
- % inhibition=vessel number of CAM treated normal saline – vessel number of CAM treated synthesized compound / vessel number of CAM treated normal saline X 100

Table.No.14

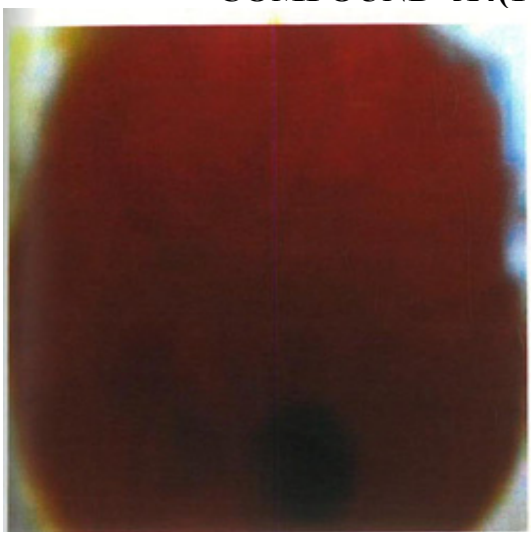
COMPOUND	% INHIBITION	
	50µg/ml	**100µg/ml**
A4	45.3	62.5
A7	53.7	76.1

IN VIVO – ANTI ANGIOGENESIS

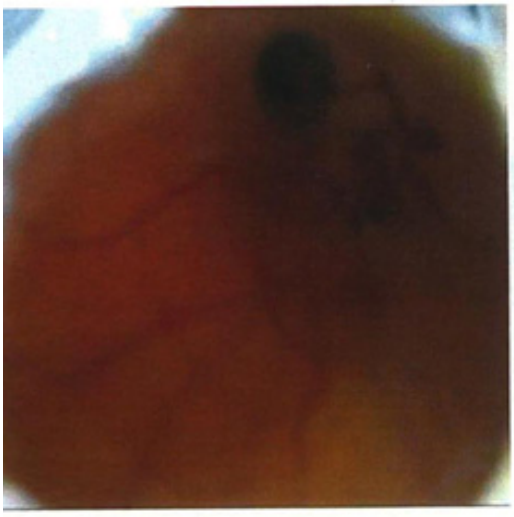
COMPOUND A4(50µg/ml)



COMPOUND A4(100µg/ml)

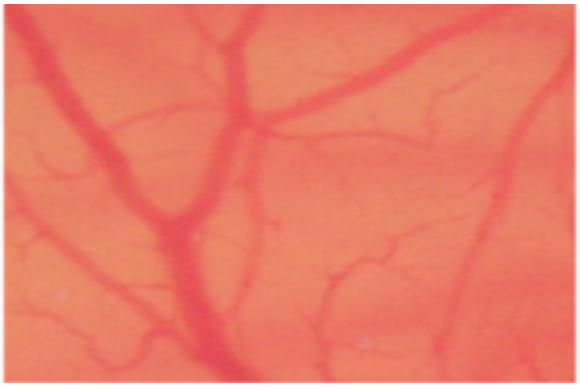


COMPOUND A7(50µg/ml)



COMPOUND A7(100µg/ml)

CONTROL



RESULTS & DISCUSSION

Results and Discussion

- The molecular design of synthesized compound were done by using different software.
- The lipinskin rule was predicted for all synthesized compound using CHEMDOODLE. The results were shown in **Table.No:1**
- The molecular formula,molecular weight and I.U.P.A.C name are predicted and shown in **Table.No:2**
- The pecentage yield, melting point, solubility and appearance of the compound are determined and shown in **Table.No;3**
- The purity of the compounds were checked by TLC and Rf value was calculated. The results are shown in **Table.No:4**
- Elemental compostion were found and calculated in percentage and results obtained were shown in **Table. No:5**
- The structure of the synthesized compounds were confirmed by IR spectraNMR spectra and Mass spectra.
- IRspectra interpert value shown in **Table**.**No:6**
- NMR specctra interpert value shown in **Table**.**No:7**
- Mass spectra results are shown in **Table.No.8**
- All synthesized compounds were screened for their *invitro* antimicrobial, antioxidant, anti arthritic and *in vivo* anti angiogenesis activiy.
- The antibacterial activity was performed against bacillus subtilis, klebsiella pneumonia. The zone of inhibition was performed by cup-plate method and results are obtained were measured in milimeter shown in **Table.No:9**

- The graphical representation compound were shown and compared with the standard Amikacin.
- The antifungal activity was performed against candida albicans,aspegillus niger. The zone of inhibition was performed by cup-plate method and results are obtained were measured in milimeter shown in **Table.No:10**
- The graphical representation compound were shown and compared with the standard Ketakonazole.
- The maximum zone of inhibition of synthesized compound against antimicrobial activity shown in **Table.No:11**
- All synthesized compound were tested for *invitro* anti oxidant activity by reducing power assay method in different concentration and compared with the standard Ascorbic acid. The result are shown in **Table.No:12**
- All of the newly obtained compound were tested for *invitro* anti arthritic activity by protein denaturated method in different concentration and compared with the standard Diclofenac. The results are shown in **Table.No:13**
- The synthesized compounds of A4 and A7 were screened for *in vivo* anti angiogenesis activity using chorioallantoic membrane neovascularisation model in the fertilized chicken eggs. The results are shown in **Table.No:14**

SUMMARY & CONCLUSION

SUMMARY AND CONCLUSION

- Preliminary screening of novel **2,4,5 triphenyl derivative** was done by using chemdoodle and molinspiration software.
- The synthesized compounds were found to be identified by **TLC.**
- All synthesized compounds were purified and characterized by the **IR,NMR and MASS** spectrals datas.
- The spectral datas were coinciding with the structure of synthesized compounds.
- All the relevant peaks were identified in all the spectras.
- The synthesized compounds were screened for *invitro* antimicrobial, anti oxidant, antiarthritic activity and *in vivo* antiangiogenesis activity.

♦ ***In vitro* Antimicrobial activity**:

The**compound A7** shows potent antibacterial activity against bacillus subtilis and Klebsiella pneumonia compared to standard Amikacin.

The **compound A9& A10** shows moderate antifungal activity against candida albicans compared to standard ketokonazole.The **compound A7** minimum inhibition of antifungal activity against aspergillus niger compared to standard Ketokonazole.

♦ ***In vitro* Antioxidant acivity**:

The following **compounds A7,A9, A10** are reducing the free radicals and prevent the tissue damage and producing best anti oxidant properties which is evaluated by reducing power assay. When it is compared to standard like Ascorbic acid these are shows lesser activity.

- ***In vitro* Antiarthritic activity**:

  Synthesized compounds like **A4,A7,A8,A9,A10** are control the risk of arthritic. It was controlled by protein denaturation. Through this studies **compound A8** shows excellent anti arthritic activity compared to the standard Diclofenac.

  In future we can carry out the in vivo studies in these compound ultimately we should confirm the anti arthritic activity.

- ***In vivo* anti angiogenesis activity**:

  Compound **A4,A7** are block blood vessels formation in the chorioallantoic membrane. It was identified the neovascularisation model in the fertilized chicken eggs. It can be acknowledge by photo copies of chrioallantoic membrane.

  In future if it is possible to alter the compound by substitution. While it expose the good anti canceractivity also.

  - **Compound A7[** 5-(4-chlorophenyl)2,4, Diphenyl -1H imidazole 1-yl piperzine] having *in vitro* Anti microbial, Antioxidant, Antiarthritic and *in vivo* Antiangiogenesis activity, As per my knowledge I conclude that **compound A7[5-(4-chlorophenyl)2,4, Diphenyl -1H imidazole 1-yl piperzine]** is the best compound compare than other than nine compounds.

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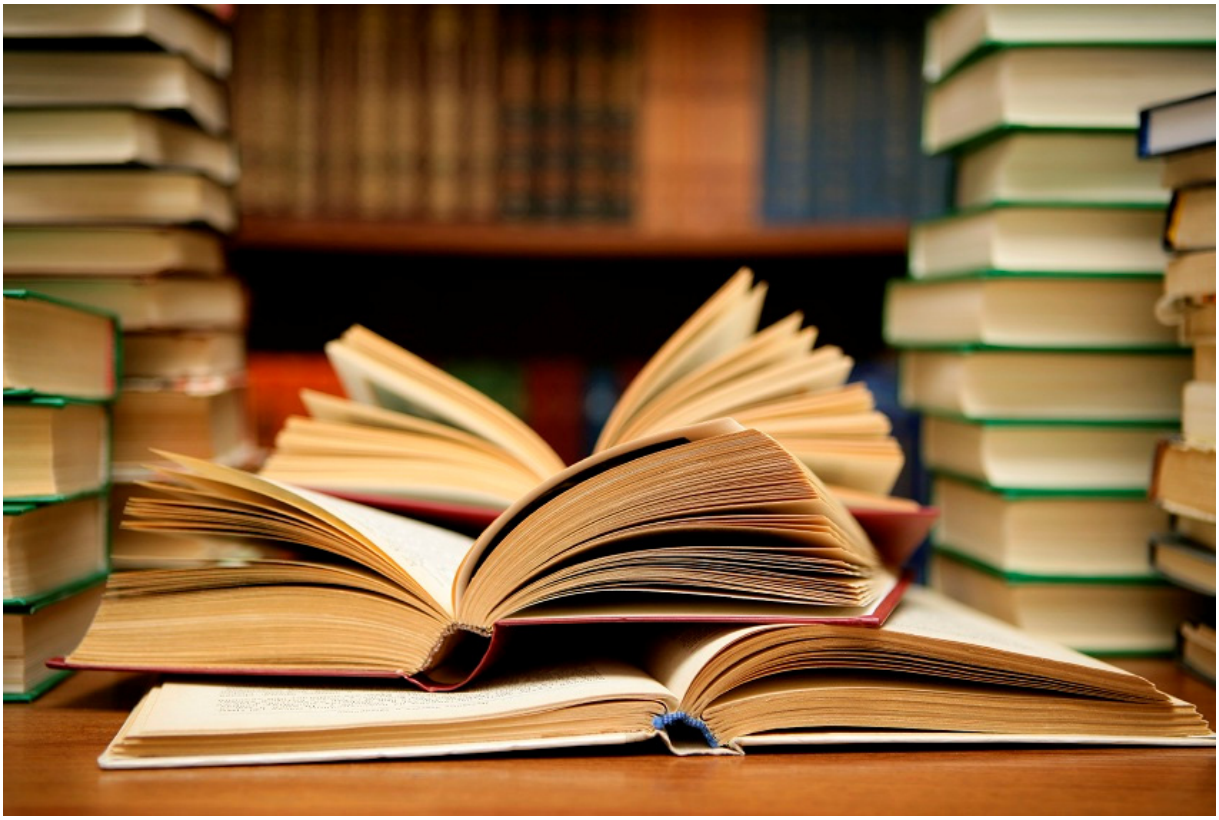

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THANK YOU